A CLINICAL STUDY ON PRESENCE OF HYPOTHYROIDISM IN DIAGNOSED PATIENTS OF GALLSTONE DISEASES

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POSTGRADUATE IN GENERAL SURGERY

DISSERTATION SUBMITTED TO

B. L. D. E. (Deemed to be University)'s SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA, KARNATAKA

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ABBREVIATIONS

GB	-	Gall Bladder
CBD.	-	Common Bile Duct
SO	-	Sphincter of Oddi
CCK	-	Cholecystokinin
USG	-	Ultrasonogram
CECT	-	Contrast Enhanced Computed Tomography
MRCP	-	Magnetic Resonance Cholangio Pancreaticography
ERCP	-	Endoscopic Retrograde Cholangiopancreaticography
PTC	-	Percutaneous Transhepatic Cholangiography
TSH	-	Thyroid Stimulating Hormone
TH	-	Thyroid Hormones
TR	-	Intranuclear Thyroid Receptors

ABSTRACT

TITLE: A CLINICAL STUDY ON PRESENCE OF HYPOTHYROIDISM IN DIAGNOSED PATIENTS OF GALLSTONE DISEASES

AIM:

To assess the correlation of hypothyroidism in patients diagnosed with cholelithiasis / choledocholithiasis.

OBJECTIVES:

1. To assess and measure the clinical and biochemical parameters to diagnose hypothyroid patients with cholelithiasis / choledocholithiasis
2. To correlate significance of hypothyroidism in cholelithiasis / choledocholithiasis

MATERIALS AND METHODS: All patients who attended outpatient and admitted in Department of Surgery at B.L.D.E. (D. U)'S Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapura, diagnosed with gallstone diseases were evaluated for the presence of hypothyroidism.

- This was a Cross sectional study conducted from April 2023 to January 2025.
- Sample size – 110
- Patients of any gender or age group diagnosed with cholelithiasis / choledocholithiasis were included.
- Patients with known thyroid disorders on treatment, or who underwent thyroid surgeries were excluded.
- Patients underwent detailed history taking, examination and necessary investigations and diagnosed with cholelithiasis/choledocholithiasis.
- These patients underwent appropriate management and intervention as per standard protocols.
- In addition, these patients underwent evaluation of their thyroid profile, (serum T3,T4, and TSH levels), before starting of treatment.

RESULTS: Out of 110 patients, 65 were women & 45 were men. 14% were around <30 years,20% around 31-40years, 40% around 41-60years,26% were over 60years of age. Fifteen patients 15(13%) were found to have hypothyroidism. while 95 patients (87%) were euthyroid. Among the 15 patients 11 were women.

CONCLUSION: Subclinical hypothyroidism as a potential precipitating factor in patients diagnosed with gallstone diseases should be considered and treated appropriately.

All patients with gallstone disease should be evaluated for possible presence of thyroid diseases so that early intervention can be initiated.

INTRODUCTION

The disease of gallstones is very prevalent among biliary disorders. It is associated with considerable morbidity and mortality. In India, its prevalence varies significantly, with North Indians showing a 2- to 4-fold higher rate compared to the South Indian population. The type of stones also differs geographically—cholesterol stones are more common in Western countries, whereas pigment stones are more frequently observed in Asian and Indian populations, particularly in South India. Gallstones may be solitary or multiple, and based on their composition, they can appear radiolucent or radio-opaque on imaging. A key mechanism in cholesterol stone formation involves the supersaturation of bile with cholesterol, initiating crystal nucleation. In contrast, pigment stones are primarily linked to biliary stasis and infection. Factors such as the function of the sphincter of Oddi, hepatic bile clearance, and various mechanical influences also contribute to gallstone development.

Hypothyroidism is also common, often remaining subclinical and undiagnosed. There is a notable overlap in the populations affected by both gallstone disease and hypothyroidism, as thyroid hormone activity plays a role in the pathogenesis of gallstones.[1,2]

Thyroid hormones exert a pro-relaxant effect on the sphincter of Oddi through the presence of thyroxine receptors. In hypothyroid states, reduced thyroid hormone levels result in increased sphincter tone and elevated biliary pressure, leading to biliary stasis. These physiological changes contribute to the development of biliary stasis in patients with hypothyroidism. Assessing the incidence of hypothyroidism among individuals with gallstone disease may provide further insight into the potential correlation between the two conditions. [3,4]

AIMS AND OBJECTIVES OF THE STUDY:

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REVIEW OF LITERATURE

EMBRYOLOGY: [5,6]

During the 4th week of embryonic life, the gall bladder, bile ducts, and liver begin to develop from a ventral bud at the most caudal aspect of the foregut. This bud is termed as the hepatic diverticulum. The ventral mesentery contains layers which in between, grows the hepatic diverticulum.

This hepatic diverticulum consists of two components namely:

1. pars hepatica and
2. pars cystica.

Pars hepatica is the most cranial component. It develops into the liver, intrahepatic bile ducts, and the common hepatic duct.

The pars cystica is the most caudal component and it develops into the cystic diverticulum, which serves as the anlage of gall bladder and cystic duct.

The common bile duct emerges as the hepatic diverticulum elongates. These structures first seem as solid cord, and eight weeks of gestation help to develop the lumen along the biliary tract.

GROSS ANATOMY:

GALLBLADDER[7-10]

It is a thin walled, flask-shaped, blind-ending diverticulum. The cystic duct connects the gall bladder to the bile duct. It functions to store and concentrate bile. In life, the gall bladder appears grey-blue. Usually located between segments IV and V at the lower end of the major plane, the gall bladder is tightly attached by connective tissue to the inferior surface of the right lobe of the liver.

In adults, the gall bladder measures between 7 and 10 cm in length. It has a resting volume of about 25 ml and a maximum capacity of up to 50 ml. It typically occupies a shallow fossa known as the gallbladder bed on the visceral aspect of the right lobe of

the liver, enveloped by peritoneum extending from the surface of the liver. This attachment can vary significantly; in rare cases, The gallbladder may be predominantly encased within the liver, termed an ‘intrahepatic gallbladder,’ or suspended by a peritoneal mesentery, known as the “mesenteric pattern,” which can pose a risk of torsion. Occasionally, it may be connected to the duodenum by an extension of the free edge of the lesser omentum, known as the cystoduodenal ligament. The gallbladder is usually situated near the duodenum, pylorus, hepatic flexure of the right colon, and right kidney.

Anatomically, the gall bladder is described as having three parts: the fundus, the body, and the neck. The neck is located at the medial end near the porta hepatis and usually has a short peritoneal attachment (mesentery) to the liver. This contains the cystic artery. The mucosa on the medial aspect of the neck exhibits oblique ridges, creating a crescentic fold that links to the spirally structured mucosal folds within the cystic duct. The neck expands laterally to constitute the body of the gallbladder, known as 'Hartmann's pouch.'

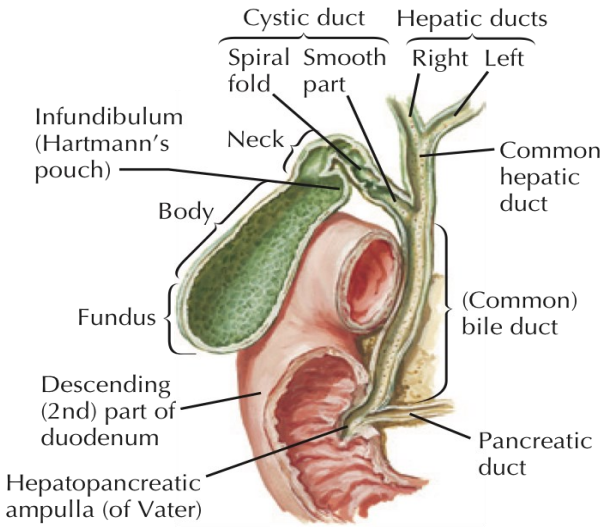

Fig:1 Gallbladder [9]

The gall bladder is anatomically subdivided into fundus, body and neck. The neck ends in an infundibulum which is narrow.

FUNDUS:

The fundus is the rounded, non-communicating section of the gallbladder that protrudes slightly beyond the acute inferior margin of the liver. It is elongated and highly mobile, orientated downward, forward, and to the right, occupying a cystic notch in the liver's edge. The fundus, when distended, abuts the parietal peritoneum of the anterior abdominal wall, located posterior to the right 9th costal cartilage at the intersection of the transpyloric plane and the right costal margin, adjacent to the lateral edge of the right rectus sheath. The fundus is generally positioned next to the transverse colon, slightly to the left of the hepatic flexure. The gallbladder's least vascularised region is particularly vulnerable to ischaemic alterations, including perforation.

BODY:

The body comprises the predominant portion of the gallbladder, orientated superiorly, posteriorly, and laterally towards the right extremity of the porta hepatis. It typically rests against the liver's visceral surface, with its superior aspect associated with the liver and its inferior aspect connected to the right segment of the transverse colon, extending posteriorly to the superior section of the duodenum and the proximal segment of its descending portion. The body is positioned anterior to the second segment of the duodenum and the right extremity of the transverse colon.

NECK:

The neck is a constricted segment near the superior extremity of the gallbladder, located between the body and the cystic duct. It ascends and advances before abruptly reversing and descending to merge with the cystic duct. In a normal anatomical position, the neck of the gallbladder is situated superior to the fundus, adjacent to the free margin of the smaller omentum. There is a constriction at the intersection of the cystic duct. The neck is connected to the liver via areolar tissue, which encompasses the cystic artery.

INFUNDIBULUM:

The infundibulum is a little bulbous diverticulum of the gallbladder, generally situated on the inferior aspect of the right wall of the neck. It extends inferiorly and posteriorly

towards the duodenum and is commonly known as Hartmann's pouch, seen as a consistent characteristic of the normal gallbladder.

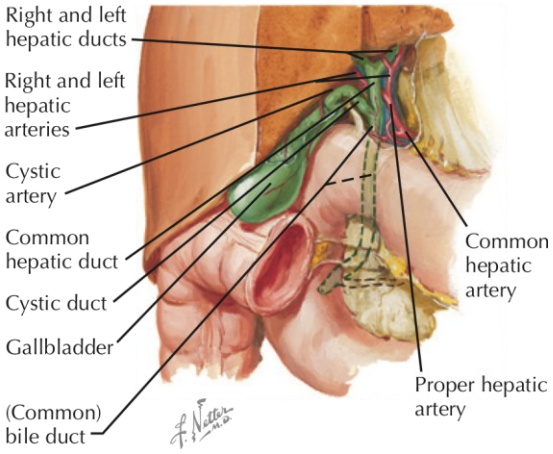

Fig:2 Gallbladder and extra hepatic ducts[9]

BILE DUCTS[7-11]

The extrahepatic biliary tree consists of the right hepatic duct, left hepatic duct, common hepatic duct, cystic duct, and the common bile duct. The left hepatic duct is longer than the right and is more susceptible to dilation from distal occlusion. The ducts converge near their exit from the liver to create the common hepatic duct, which generally measures 1 to 4 cm in length, possesses a width of about 4 mm, and is positioned anterior to the portal vein and to the right of the hepatic artery.

The cystic duct departs from the gallbladder and converges with the common hepatic duct at an acute angle, creating the common bile duct. The portion of the cystic duct around the gallbladder neck has variable mucosal folds referred to as the spiral valves of Heister, which, despite lacking genuine valvular function, may complicate cannulation.

The cystic duct's length and trajectory may differ, being short, nonexistent, or running parallel and spiraling around the common hepatic duct before converging with it, occasionally as distally as the duodenum. Variations in the cystic duct and its confluence with the common hepatic duct are of surgical importance, as misidentification may result in bile duct damage..

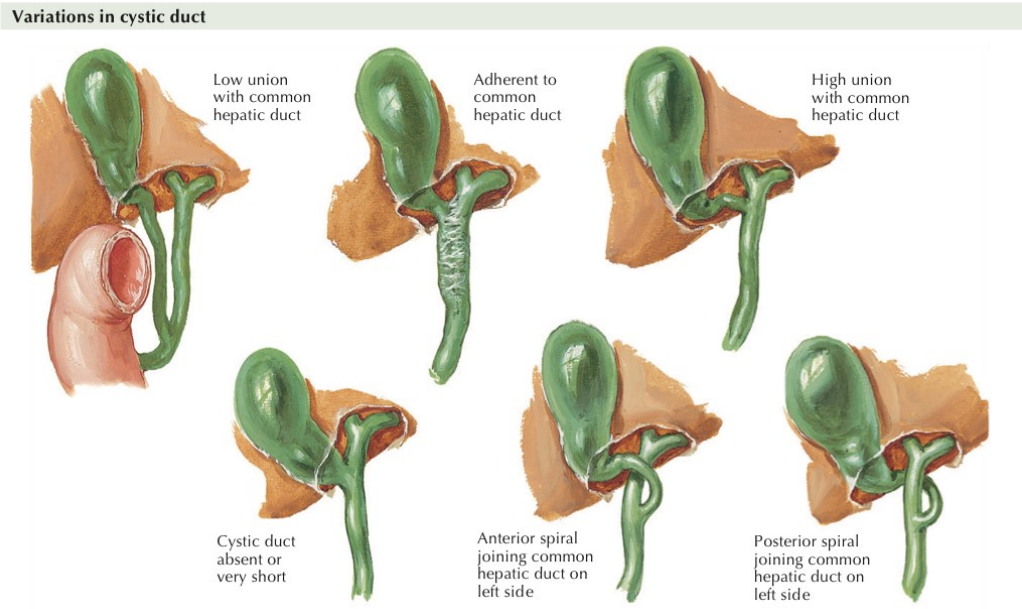

Fig:3 variations in cystic duct[9]

The confluence of the cystic duct and common hepatic duct signifies the commencement of the common bile duct, which generally measures between 7 to 11 cm in length and 5 to 10 mm in diameter, with the diameter potentially enlarging with age and post-cholecystectomy.

The superior third (supraduodenal segment) descends within the hepatoduodenal ligament. Its position is to the right of the hepatic artery. This segment lies anterior to the portal vein. The middle third (retroduodenal segment) arcs posteriorly to the initial section of the duodenum, diverging laterally from the portal vein and hepatic arteries. The inferior third (pancreatic segment) may arch posteriorly or pass through the head of the pancreas prior to penetrating the wall of the second half of the duodenum. It descends obliquely within the duodenum wall for 1 to 2 cm before terminating at the ampulla of Vater, situated around 10 cm distal to the pylorus.

The confluence of the common bile duct and the main pancreatic duct exhibits three configurations: in approximately 70% of individuals, they merge externally to the duodenal wall and enter as a singular duct; in around 20%, they converge within the wall, presenting a short or absent common duct; and in about 10%, they exit through distinct orifices, referred to as pancreas divisum. The sphincter of Oddi, consisting of a robust layer of circular smooth muscle, encircles the common bile duct at the ampulla of Vater, controlling the passage of bile and, in certain instances, pancreatic juice into the duodenum.

The extrahepatic bile channels are coated with columnar mucosa that houses numerous mucous glands, especially abundant in the common bile duct. The mucosa is encased in fibroareolar tissue containing few smooth muscle cells; a separate muscle layer is absent in the human common bile duct. The vascular supply originates from the gastroduodenal and right hepatic arteries, with principal trunks traversing the medial and lateral walls of the common duct. The innervation of thecommon bile duct parallels that of the gallbladder, exhibiting a heightened concentration of nerve fibres and ganglia adjacent to the sphincter of Oddi.

Calot's triangle:[12]

It is often referred to as the hepatobiliary or cystohepatic triangle.

The superior border is delineated by the inferior surface of the liver, whereas the inferior border is constituted by the cystic duct and medially by the common hepatic duct. The Calot triangle principally encompasses the cystic artery, the lymph node of Lund, and the auxiliary right hepatic artery. Accessory hepatic ducts may infrequently be observed in the triangle.

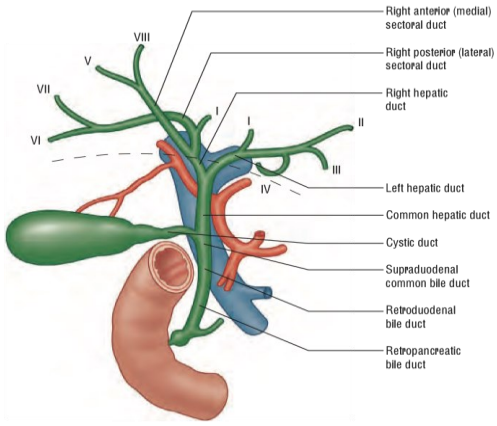

Fig:4 Calot's triangle [7]

The common bile duct, approximately 7.5 cm in length, originates by the convergence of the cystic and common hepatic ducts.

It is situated in the interiors of the hepatoduodenal ligament and to the right of the hepatic artery. The common bile duct is anteriorly related to the portal vein. It is split into four sections. The supraduodenal segment, approximately 2.5 cm long, traverses the free margin of the inferior omentum. The retroduodenal segment is situated

posterior to the second half of the duodenum. The infra duodenal segment is situated within a groove on the neck of the pancreas.

The intra duodenal segment traverses obliquely through the wall of the second half of the duodenum and enters the duodenum near the apex of the papilla of Vater. This structure encircles the bile duct orifice and consists of duodenal tissue and muscular components, forming the sphincter of Oddi. Typically, a shared channel exists where the pancreatic duct and distal common bile duct converge, discharging through a single orifice into the duodenum. This prevalent pathway is considered significant in the development of gallstone pancreatitis.

HISTOLOGY OF GALLBLADDER:[7-11]

The gallbladder consists of three distinct histological layers: serosal, fibromuscular, and mucosal layers.

Serosal Layer: The serosal layer originates from the peritoneum, fully enveloping the fundus of the gallbladder, but only partially covering the inferior surface and lateral aspects of the body and neck. Below this layer is the subserosal layer, composed of areolar tissue.

Fibromuscular Layer: This thin layer consists of fibrous tissue interspersed with smooth muscle fibres, organised into loose bundles. The fibres are arranged in longitudinal, circular, and oblique orientations, forming a crisscross pattern, most prominent in the neck of the gallbladder.

Mucosal Layer: The mucosal layer is tenuously attached to the fibromuscular layer and features recesses termed the crypts of Luschka, which penetrate into the muscular coat. The epithelium has a monolayer of columnar cells. The mucosa in the neck predominantly serves an absorptive function, while also secreting mucus.

HISTOLOGY OF CYSTIC DUCT AND BILE DUCT: [7-11]

The mucosa of the cystic duct is raised into 5 to 12 crescentic folds, referred to as the "Valves of Heister," which are crucial for the movement of bile into and out of the gallbladder. Microscopically, the bile duct layers are analogous to those of the gallbladder.

The external fibromuscular layer of the bile duct has robust connective tissue fibres interspersed with little muscular components, with density augmenting in the distal segments. The mucosa consists of a singular layer of columnar epithelium.

Electron microscopic investigations have identified microvilli and cilia on the apical membrane of ductal cells, which are considered essential for the mixing and motility functions of the duct..

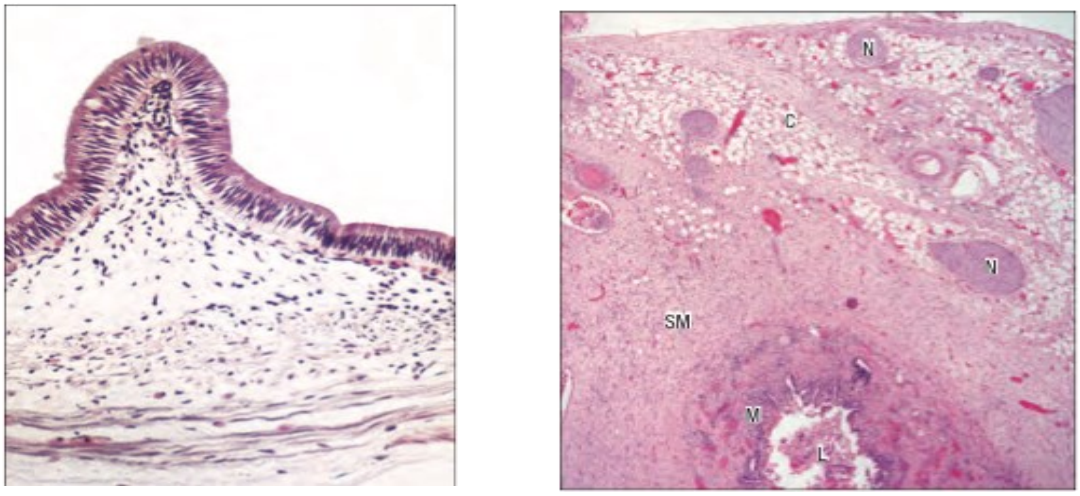

Fig:5 Histology [7]

VESSELS AND LYMPHATICS [7-11]

ARTERIAL SUPPLY

The anatomy of the arterial supply to the gallbladder and bile ducts is highly variable and critical to understand, particularly in surgeries like cholecystectomy.

GALLBLADDER

- Cystic artery

The cystic artery generally originates from the right hepatic artery, which itself arises from the hepatic artery proper, a branch of the common hepatic artery stemming from the coeliac axis.

The course and origin of the cystic artery can vary significantly, which is important during surgical procedures.

Variants include origins from:

- Common hepatic artery
- Left hepatic artery
- Superior mesenteric artery

It may pass either anterior or posterior to the hepaticor bile ducts.

BILEDUCT:

- Posterior superior pancreaticoduodenal artery, retroduodenal artery, and the right and left hepatic arteries.

- All these branches ultimately arise from the celiac axis.During procedures like a cholecystectomy, these variations are critical to avoid vascular injury and complications.

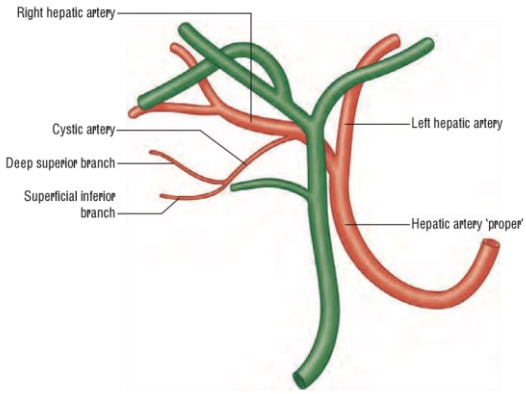

Fig:6 Cystic and Hepatic Arteries[7]

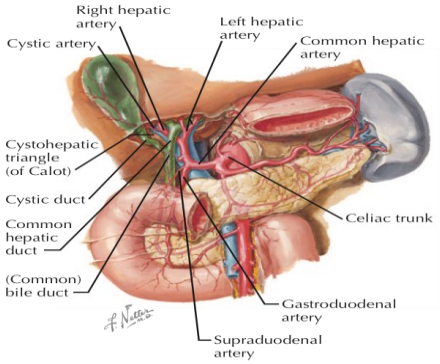

Fig:7 Biliary system arteries[9]

VENOUS DRAINAGE

Cystic Veins

- Veins from the body of the gallbladder typically pass directly into the liver, draining into the hepatic sinusoids.
- Veins from the neck of the gallbladder and cystic duct generally drain into the right portal venous system.
- Some veins also drain the biliary duct system.

LYMPHATIC DRAINAGE

- Cystic lymph nodes cluster around the neck of the gallbladder.
- Lymph from the cystic region also drains into the hepatic nodes around the upper bile duct.

- Deeper lymphatic drainage continues into the celiac nodes located around the celiac arterial trunk.

NERVE SUPPLY:

The innervation of the gallbladder is rich and complex, involving both sympathetic and parasympathetic components, which influence its function. Here's a detailed breakdown:

Innervation of the Gallbladder:

- Parasympathetic fibers:

Primarily arise from the hepatic branch of the anterior vagal trunk.

They stimulate gallbladder contraction and cause relaxation the ampullary sphincter (sphincter of Oddi), aiding in bile release into the duodenum.

- Sympathetic fibers:

Originating from the celiac ganglia, with preganglionic fibers from the T7-T9 spinal cord segments.

Sympathetic input inhibits gallbladder contraction, likely reducing bile release when digestion is not needed.

- Autonomic plexus:

A nerve plexus lies within the muscular and submucosal layers of the gallbladder, controlling its motor functions.

Referred Pain:[13]

Right phrenic nerve involvement:

- Communication between the phrenic nerve and the celiac plexus allows some fibers to reach the gallbladder through the hepatic plexus.

- This connection explains why gallbladder pathology (e.g., gallstones or inflammation) can cause referred pain to right shoulder, due to shared innervation from phrenic nerve,

which supplies the diaphragm, leading to sensation of pain in regions served by phrenic nerve.

PHYSIOLOGY:

GALLBLADDER:[7,8,13]

The gallbladder, bile ducts, and sphincter of oddi function collectively to store bile and regulate its flow into the duodenum. The gallbladder's primary role is to store and concentrate bile produced by the liver and release it in response to food intake.

ABSORPTION AND SECRETION

- During fasting, approximately 80% of hepatic bile is stored in the gallbladder.
- The gallbladder mucosa has the highest absorptive efficiency in the body, concentrating bile up to tenfold by absorbing sodium, chloride, and water—this prevents a rise in biliary pressure.
- Mucosal cells also secrete glycoproteins and hydrogen ions. Mucus protects the lining from bile and facilitates bile flow, while acidification helps prevent calcium salt precipitation that may lead to gallstones.
- In cases of cystic duct obstruction, continuous mucus production can result in "white bile," as seen in gallbladder hydrops.

MOTOR ACTIVITY:[13]

- Tonic contraction of the sphincter of Oddi during fasting maintains a pressure gradient, promoting gallbladder filling.
- During phase II of the migrating myoelectric complex (MMC), small amounts of bile enter the duodenum.
- After meals, cholecystokinin (CCK) released in response to fats, amino acids, and gastric acid induces gallbladder contraction and sphincter relaxation, releasing bile.
- The gallbladder expels 50–70% of its contents within 30–40 minutes post-ingestion and subsequently replenishes during the next 60–90 minutes..

NEUROHORMONAL REGULATION:[13]

- Parasympathetic stimulation via the vagus nerve promotes contraction; sympathetic input from the celiac plexus inhibits it.
- Substances like nicotine and caffeine stimulate contraction, while anticholinergics such as atropine inhibit it.
- Gastric antral distension also triggers gallbladder contraction and sphincter relaxation.
- CCK acts through smooth muscle receptors and vagal pathways to mediate bile release. Vagotomy can impair this response, resulting in gallbladder enlargement.
- Inhibitory agents like vasoactive intestinal peptide (VIP) and somatostatin reduce gallbladder motility. Chronic inhibition, as in somatostatinoma, is associated with increased gallstone risk.

SPHINCTER OF ODDI:[13]

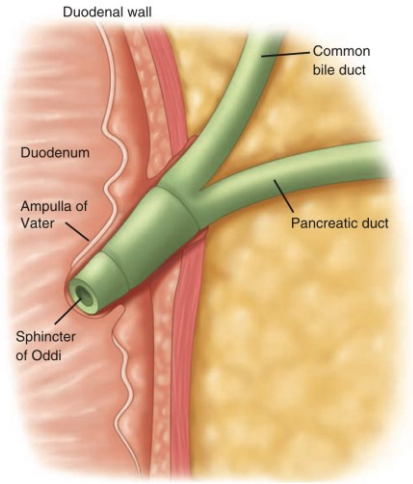

Fig:8 Sphincter of Oddi (14)

Function:

The sphincter of Oddi plays a crucial role in biliary and pancreatic regulation by doing the following:

1. Controls the bile flow and pancreatic secretions into the duodenum.
2. Preventing the backflow of duodenal contents into the biliary system.
3. Creating a high-pressure zone between the bile duct and the duodenum, which diverts bile into the gallbladder for storage during fasting.

Anatomically, the sphincter measures 4–6 mm in length and maintains a basal pressure approximately 13 mmHg above that of the duodenum. It exhibits phasic contractions at a rate of four per minute, with contraction amplitudes ranging between 12 and 140 mmHg.

Regulation of Activity:

- ✓ The sphincter's motility is coordinated by the interstitial cells of Cajal and modulated by intrinsic and extrinsic neural and hormonal inputs.
- ✓ Hormones such as cholecystokinin (CCK), glucagon, and secretin relax the sphincter by decreasing contraction strength and basal tone, thereby promoting bile flow into the duodenum.
- ✓ During fasting, sphincter function is synchronized with the migrating myoelectric complex (MMC), which regulates periodic bile release.
- ✓ Pharmacologic agents like glucagon are used clinically to reduce sphincter pressure temporarily for diagnostic procedures.

This intricate coordination between hormonal, neural, and muscular systems ensures precise bile storage and release, optimizing digestion and preventing complications like gallstone formation.

The gallbladder, bile ducts, and sphincter of Oddi work in unison to store, concentrate, and deliver bile in response to food intake.

PHYSIOLOGY OF BILE PRODUCTION AND FLOW

BILE SECRETION AND COMPOSTION [15-19]

Bile is produced in the hepatic lobules and released into a system of canaliculi, which converge into bile ductules and subsequently bigger ducts that accompany the portal vein and hepatic artery. The interlobular ducts coalesce to create septal ducts, which ultimately unite into the right and left hepatic ducts. The ducts converge to create the common hepatic duct.

The common bile duct (CBD) is formed when the common hepatic duct merges with the cystic duct from the gallbladder. The CBD usually reaches the duodenum via the pancreatic duct through the ampulla of Vater.

Hepatic bile is an isotonic fluid that resembles plasma in composition. In the gallbladder, bile is concentrated through the active reabsorption of water, chloride, and bicarbonate. This mechanism elevates the solute concentration from 3–4 g/dL in hepatic bile to 10–15 g/dL in gallbladder bile that is stored.

The following form the major components of bile:

- ✓ Bile acids (80%)
- ✓ Lecithin and other phospholipids (16%)
- ✓ Cholesterol (4%)

In lithogenic states, the cholesterol concentration in bile can increase to 8–10%, contributing to gallstone formation. Besides cholesterol, bile also contains conjugated bilirubin, proteins such as albumin and immunoglobulins, electrolytes, mucus, and occasionally drug metabolites.

On average, the liver secretes about 500–600 mL of bile daily. Components like phospholipids and bile acids are either synthesized by hepatocytes or reabsorbed from circulation before being secreted into the bile.[16-19]

Bile Flow Regulation:

Three main mechanisms regulate bile flow:

1. Active transport of bile acids from hepatocytes into bile canaliculi.
2. Active transport of organic anions.
3. Cholangiocellular secretion.

BILE ACIDS [20]

- Primary bile acids, namely cholic acid and chenodeoxycholic acid (CDCA), are synthesised from cholesterol in the liver and subsequently conjugated with glycine or taurine prior to their secretion into bile.
- Secondary bile acids (e.g., deoxycholate and lithocholate) are produced in the colon from primary bile acids by bacterial metabolism.
- Lithocholate is poorly absorbed compared to deoxycholate.
- Ursodeoxycholic acid (UDCA), a stereoisomer of CDCA, is present in small amounts.
- The glycine to taurine conjugate ratio is typically 3:1 in healthy individuals.
- Bile acids have detergent-like properties and form micelles when present above a critical concentration (~2 mM). This is essential for cholesterol solubilization in bile, as cholesterol alone is poorly soluble. Normal bile acid-to-lecithin ratios prevent cholesterol precipitation, while abnormal ratios can promote gallstone formation.
- Bile acids also aid in the absorption of dietary fats and fat-soluble vitamins in the intestine and play a key role in regulating bile flow, water, and electrolyte transport in the intestine.

ENTEROHEPATIC CIRCULATION:[20,21]

- The liver produces only a small portion of the total bile salt pool used daily due to the enterohepatic circulation, in which bile salts are recycled.
- Both conjugated and unconjugated bile acids are passively absorbed throughout the gut.
- Active transport of conjugated bile acids occurs primarily in the distal ileum.

- Reabsorbed bile acids return to the liver via the portal circulation, where they are reconjugated and resecreted into bile. This cycle happens 5-10 times daily.
- The total bile acid pool is 2-4 g, and 95% of bile acids are reabsorbed, resulting in a fecal loss of only 0.2-0.4 g/day. The liver compensates for this loss by synthesizing an equivalent amount of bile acids daily.
- By decreasing the activity of the rate-limiting enzyme CYP7A1, fibroblast growth factor 19 (FGF19), which is released in response to bile acids in the intestine, travels to the liver and prevents the synthesis of bile acids. Additionally, FGF19 encourages gallbladder relaxation.
- The liver can synthesize up to 5 g/day of bile acids, but this may not be sufficient in cases of severe impairment in bile salt reabsorption, potentially leading to a deficit in the bile acid pool.

This tightly regulated system of bile production, concentration, and flow plays a critical role in digestion and the maintenance of biliary and hepatic health.

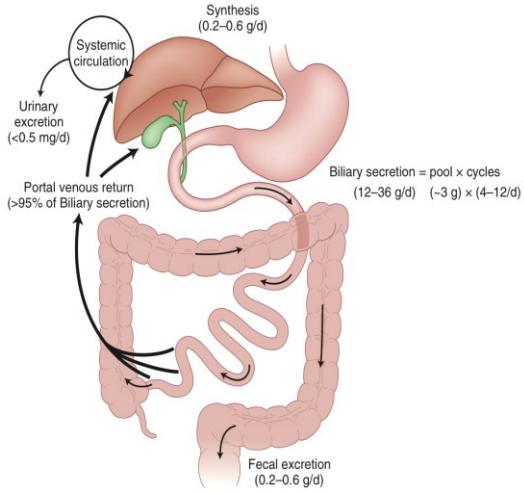

Fig:9 Enterohepatic circulation [22]

GALLSTONES [2]

Gallstones can be found in

a) gallbladder

b) extra hepatic bile duct (choleduocholithiasis)

c) intrahepatic bile ducts. (hepatolithiasis)

CLASSIFICATION OF GALLSTONES

- Inflammatory stone
- Metabolic stone
- Pure pigment- Black/ brown
- Calcium bilirubinate
- Pure cholesterin
- Combination stone
- Primary metabolic and secondary inflammatory Stasis stone
- Primary in common duct (earthy)

Japanese classification of gallstones

- Pure cholesterol stone
- Combination stone
- Mixed stone
- Pigment stone
- Black stone
- Calcium bilirubinate stone
- Rare stone [2]

PATHOGENESIS AND TYPES OF GALLSTONES [22-24]

I. Cholesterol stones:

- Pure cholesterol stones are rare, comprising less than 10% of all gallstones. Typically, they are large, smooth, and occur as single stones.
- Mixed cholesterol stones are more common, containing at least 70% cholesterol by weight, along with varying amounts of bile pigments and calcium. These stones tend to be multiple and vary in size, hardness, and shape. They may be hard and faceted or irregular, multilobed, and soft.
- The color of cholesterol stones can range from whitish-yellow to green or black. The majority of cholesterol stones (>90%) are radiolucent (invisible on X-rays), but stones with a high calcium carbonate content can become radio-opaque and visible on imaging.

Formation of Cholesterol Stones:

- The formation of cholesterol stones is primarily driven by the supersaturation of bile with cholesterol.
- Cholesterol is nonpolar, and its solubility in bile depends on the concentrations of cholesterol, bile salts, and lecithin (the main phospholipid in bile).
- Normally, cholesterol is secreted into bile and forms soluble vesicles with bile salts and phospholipids.
- Bile becomes supersaturated with cholesterol when there is hypersecretion of cholesterol (either by excessive ingestion or faulty metabolic processing). The concentration of cholesterol starts to precipitate out of solution and form solid cholesterol stones when it surpasses the solubilising ability of phospholipids and bile salts.
- Cholesterol hypersecretion is typically the cause of supersaturation rather than a reduction in bile salts or phospholipids.

The factors contributing to formation of cholesterol stones are-

i. Supersaturation of cholesterol in bile,
ii. Nucleation of crystals in the gall bladder
iii. Impaired motility leading to defective emptying

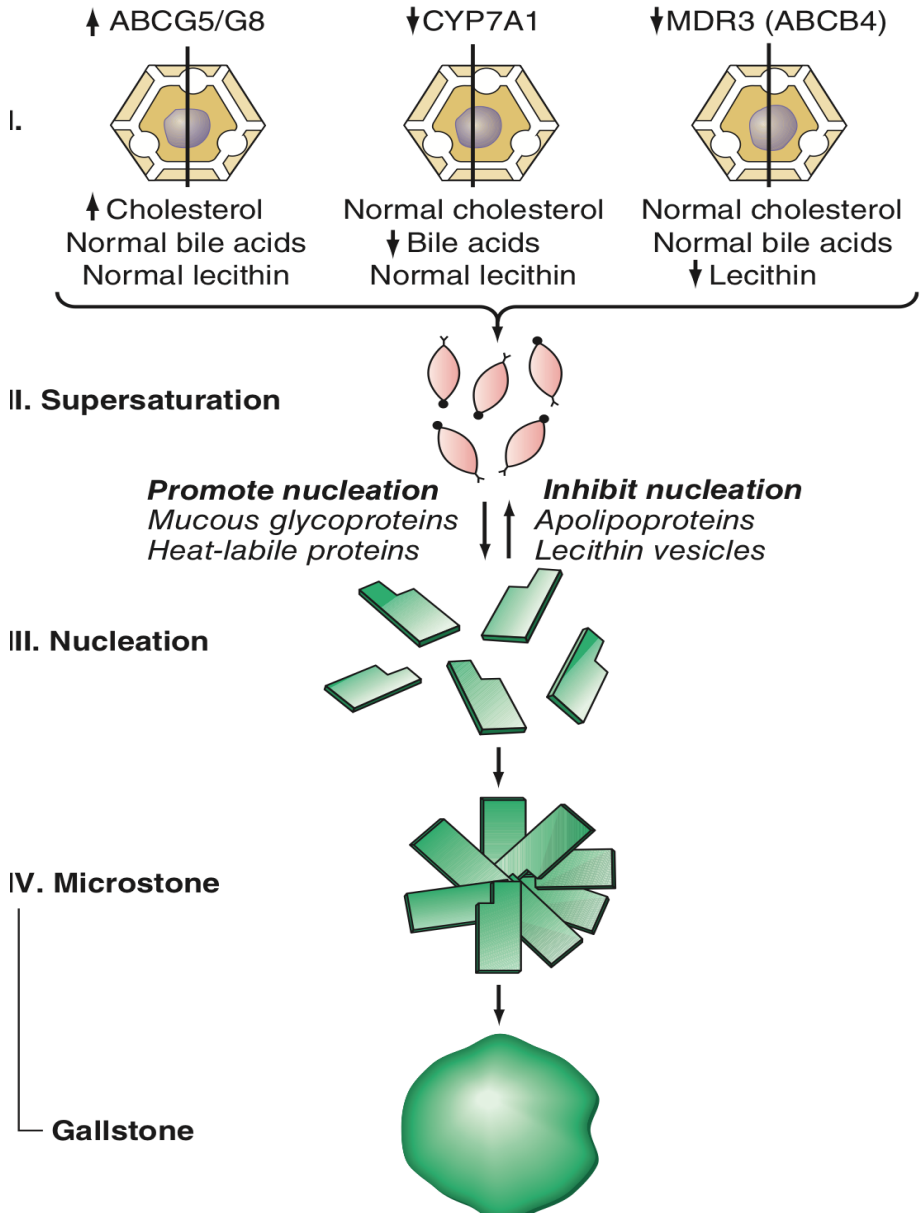

Fig:10 Formation of cholesterol stones[22]

Combination Stones:

• Combination stones originate as pure cholesterol stones but later acquire an outer layer of bile pigment. When these stones are cut open, they display a distinct two-layer structure, with an outer pigmented layer and an inner cholesterol core.

Fig:11 Cholesterol stones and mixed stones[13]

II.Pigment stones:

- Because calcium bilirubinate makes about 40–60% of the dry weight of pigment stones, they are usually black in colour and have less than 20% cholesterol.
- These stones are distinct from cholesterol stones, both in composition and formation mechanism. The cholesterol content is low (under 25-30%), and other components include calcium carbonate, calcium phosphate, and calcium fatty acids.
- Due to their calcium content, pigment stones are generally radio-opaque (visible on X-rays).

Types of Pigment Stones:[2,17]

1.Black Stones:

- Frequently linked to haemolytic conditions where there is a greater breakdown of red blood cells, such as sickle cell anaemia.
- Cross-section shows an amorphous appearance.
- These stones contain calcium carbonate and calcium phosphate.
- Appearance: Small, dark stones with a solid, often irregular surface.

2.Brown Stones:

- These stones are frequently linked to biliary stasis and subsequent bacterial infections within the bile ducts.
- Cross-section: Shows concentric layers.

- These contain calcium fatty acids, which differentiate them from black stones.
- They tend to form in cases of chronic bile duct obstruction, often in the setting of infection or parasites.

In general, pigment stones are smaller and darker than cholesterol stones and tend to form in different pathological contexts, such as hemolysis or biliary stasis with infection.

III.Mixed stones:

- Cross-section: These stones exhibit concentric and radial layers, with components of both cholesterol and pigment mixed in the layers. The cholesterol and pigment distributions vary throughout the stone.
- Shape: They range from round to faceted, depending on their composition and formation environment.
- Color: The color spectrum includes yellowish white, yellowish brown, greenish brown, and black brown, reflecting the varying concentrations of cholesterol, bile pigments, and calcium.

Mixed stones form due to a combination of cholesterol supersaturation and pigment accumulation, often as a result of multiple contributing factors such as bile stasis, infection, or metabolic disturbances.

EPIDEMIOLOGY OF GALLSTONE DISEASE [22 -24]

In many Western nations, gallstones are frequent, especially in people over 50. Gallstone prevalence in the US is 16.6% in women and 7.9% in men, per the third National Health and Nutrition Examination Survey (NHANES III). Mexican Americans have the highest prevalence (8.9% in males, 26.7% in women), followed by non-Hispanic whites (8.6% in men, 16.6% in women), and African Americans (5.3% in men, 13.9% in women) have the lowest prevalence.

RISK FACTORS:

1) Age: Gallstones are uncommon in children, except in hemolytic conditions. The incidence significantly increases after the age of 40, with individuals aged 40–69 having a fourfold higher risk compared to younger adults.[26]

2) Sex: Women are more prone to gallstones due to hormonal influences such as estrogen and the physiological changes of pregnancy.[2]

3) Family history and genetics: A strong familial predisposition exists, with gallstones occurring more than twice as frequently among family members. The risk is especially higher in females..[27]

4) Pregnancy[28] :

Multiple pregnancies elevate risk due to:

- Altered bile acid synthesis (increased chenodeoxycholic acid) reduces cholesterol solubility.
- Progesterone lowers the production of bile acids, while oestrogen increases the secretion of cholesterol.
- Progesterone slows gallbladder motility, leading to stasis and stone formation.

5) Bile excretes ceftriaxone. Ceftriaxone combines with calcium and precipitates out of bile when supersaturated, as in the case of bile stasis in patients in the critical care unit.[29]

6) Oral contraceptives and oestrogen replacement therapy: The usage of oral contraceptives is associated with a marginally elevated risk of gallstone disease. Women under 40 years of age and those utilising high-dose oestrogen preparations (exceeding 50 mcg) exhibit the highest additional risk of gallstones.[30]

7) Diabetes mellitus: This condition is not thoroughly comprehended. Hepatic insulin resistance seems to be significant.[31]

8) Obesity: It results from enhanced cholesterol synthesis and secretion. The risk is elevated in women, individuals with severe obesity, and younger age demographics.[24]

9) Rapid weight loss: This constitutes a risk factor. A low-calorie diet alters the makeup of bile. The mucin concentration in bile increases eighteenfold, whereas the calcium concentration elevates by forty percent. These conditions facilitate cholesterol nucleation and calculi development.[31]

10) Decreased physical activity: Engagement in physical exercise is associated with a diminished risk of symptomatic cholelithiasis.[32]

11) Deranged lipid profile: Gallstones are associated with elevated triglyceride levels and a decreased occurrence is observed in patients with increased high-density lipoproteins.[29]

12) Serum bilirubin: Patients with mean bilirubin levels in the greatest decile exhibited a heightened risk of symptomatic gallstone disease compared to those with lower mean bilirubin levels.[33]

13) Cirrhosis: The elevated risk may result from diminished hepatic production and transit of bile salts and unconjugated bilirubin.[29]

14) In a population study of humans without documented thyroid disease, men with raised TSH levels exhibited a 3.8-fold increased risk of cholelithiasis, whereas no such link was noted in women. The gallbladder may grow enlarged and have reduced contractility in some instances.[34]

15) Gallbladder stasis: Prolonged retention of bile in the gallbladder results in excessive cholesterol concentration, hence facilitating the production of gallstones. Examples include spinal cord injury, extended fasting resulting from normal enteral stimulation of gallbladder activity, prolonged total parenteral nutrition due to normal enteral stimulation of gallbladder activity, and patients with ileal resection, which disrupts the enterohepatic circulation of bile acids, leading to decreased hepatic bile acid secretion and consequently modifying the composition of hepatic bile. Cholesterol supersaturation, along with excess somatostatin (as seen in somatostatinoma or prolonged use of the somatostatin analogue octreotide for acromegaly and other conditions), likely inhibits gallbladder emptying by reducing cholecystokinin release.[35]

16) Other drugs: Clofibrate, bezafibrate, and other fibrates are medicines that lower cholesterol by blocking cholesterol 7-alpha-hydroxylase, the rate-limiting enzyme in bile acid production, leading to cholesterol supersaturation in bile and the formation of stones. Ceftriaxone induces the production of biliary sludge. Biliary excretion constitutes up to 40% of ceftriaxone

clearance, with drug concentrations in bile potentially reaching 200 times those of serum levels.[36]

17) Crohns' disease: These patients are susceptible to pigment gallstones, indicative of elevated levels of bilirubin conjugates, unconjugated bilirubin, and total calcium in the gallbladder bile, maybe resulting from modified enterohepatic circulation of bilirubin.[37]

18) Hemolysis: Disorders that induce haemolysis lead to the formation of pigment gallstones, including hereditary spherocytosis, sickle cell anaemia, and thalassaemia.[38]

PROTECTIVE FACTORS:[39-41]

(a) Ascorbic acid: The protective nature of the ascorbic acid is believed to be due to the effect of ascorbic acid on catabolism of cholesterol.
(b) Statins
(c) Coffee: Considered protective due to the effects of coffee on the hepatobiliary processes which lead to the formation of cholesterol gallstones.
(d) Protein and nuts
(e) Poly and monounsaturated fats: They inhibit cholesterol gallstone formation.

CLINICAL MANIFESTATIONS[2]

1. Asymptomatic:

Many gallstones are detected incidentally during routine abdominal ultrasounds, often performed for unrelated gastrointestinal complaints.

2. Nonspecific Digestive Symptoms:

Patients may report symptoms such as food intolerance, acid reflux, heartburn, bloating, constipation, or diarrhea. These symptoms often overlap with other gastrointestinal disorders and may coexist with gallstone disease.

3. Biliary Colic:

Marked by severe discomfort in the right upper quadrant or epigastric region, maybe radiating to the back or right scapular region. The discomfort generally endures for 1–5 hours, is unremitting (lacking pain-free intervals), and may be provoked by meals or disrupt sleep. Nausea and vomiting are prevalent, although fever and localised discomfort are typically absent.

4. Right Hypochondric Pain:

Persistent or episodic upper right abdominal pain, especially following fatty meals or at night, may occur even without classic biliary colic features.

5. Jaundice:

Obstructive jaundice may develop when gallstones migrate into and block the common bile duct.

6. Fever:

Fever is generally indicative of complications such as acute cholecystitis, cholangitis, or other infections associated with gallstone disease.

SIGNS[11]

1. Enlarged gall bladder: Felt as a rounded, firm swelling in the right upper abdomen, just to the side of the right rectus muscle. It descends with respiration and moves slightly side to side.

2. Right Upper Quadrant Tenderness:

Pain or discomfort is noted when pressing over the right hypochondrium.

3. Murphy's Sign:

A sudden halt in inspiration during deep palpation beneath the right costal margin, commonly observed in acute cholecystitis.

4. Boa's Sign:

Increased sensitivity to touch (hyperaesthesia) below the right shoulder blade, also associated with acute cholecystitis.

INVESTIGATIONS

1. Plain X-ray abdomen: This X-Ray shows only radio-opaque stones as marked in the figure.[43]

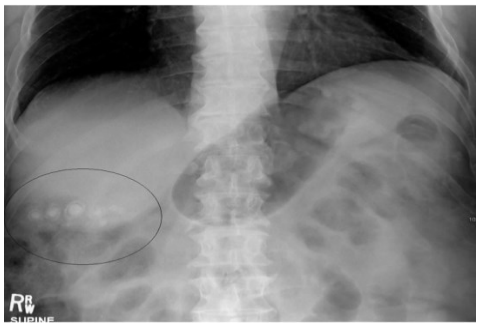

Fig:12 X-ray erect abdomen (42)

2. Oral cholecystography: In this procedure, the patient is given a fatty meal the day before, followed by six tablets of Telepaque (a contrast agent). After 12–16 hours, abdominal X-rays are taken in both erect and supine positions. Since only about 10% of gallstones are radiopaque, most (90%) are not directly visible and appear as translucent areas against the contrast-filled gallbladder.

3. Abdominal ultrasonography: This is a commonly used investigation. It is considered the investigation of choice. It can even detect asymptomatic gallstones.[43]

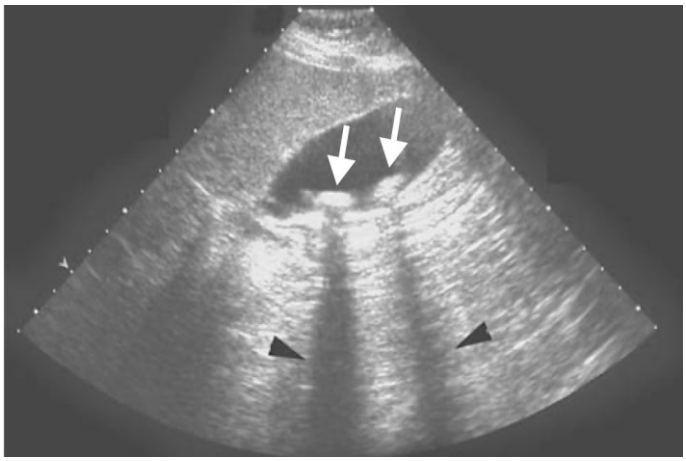

Fig:13 Ultrasonography(42)

4. CT abdomen[43] : This imaging modality offers greater detail than ultrasonography and can identify gallstones that may not be visible on ultrasound. It helps delineate the anatomy and condition of the extrahepatic biliary tree and nearby structures, aiding in the assessment of other potential causes for the patient's symptoms. CT scanning is also the preferred initial investigation for suspected malignancies involving the gallbladder, extrahepatic bile ducts, or adjacent organs like the pancreatic head. Additionally, it plays a crucial role in the differential diagnosis of obstructive jaundice when the underlying cause is unclear.

5. MRCP[43]: Magnetic resonance imaging combined with magnetic resonance cholangiopancreatography (MRCP) provides a targeted, noninvasive approach for diagnosing diseases of the biliary and pancreatic systems. It is the preferred imaging technique for detailed assessment of ductal abnormalities, with endoscopic retrograde cholangiopancreatography (ERCP) now primarily reserved for therapeutic interventions rather than diagnosis.

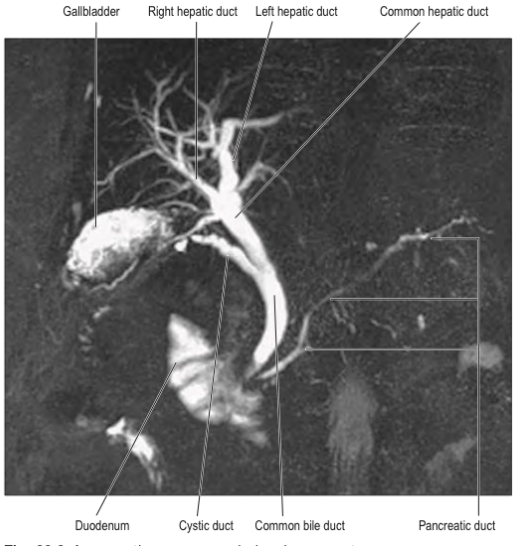

Fig:14 magnetic resonance cholangiopancreatography [7]

6) Hepatobiliary Scintigraphy[48] . Biliary scintigraphy is primarily used to diagnose acute cholecystitis. In this condition, the gallbladder fails to visualize on the scan, while the common bile duct and duodenum show normal tracer uptake. This absence of gallbladder filling is caused by inflammation-induced obstruction of the cystic duct, which blocks bile from entering the gallbladder.

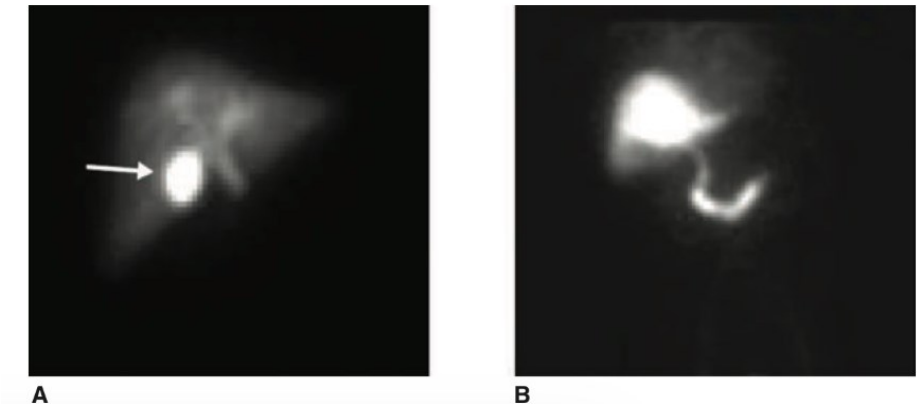

Fig:15 Hepatobiliary Scintigraphy [48]

7. ERCP: ERCP is valuable for diagnosing ductal stones and, when combined with extracorporeal shock wave lithotripsy (ESWL), can also aid in their treatment. In conditions like choledocholithiasis, obstructive jaundice, biliary strictures, or cholangitis, ERCP offers the dual benefit of diagnosis and therapy. If stones are detected on the endoscopic cholangiogram, procedures such as biliary sphincterotomy and stone extraction can be performed to effectively clear the common bile duct.

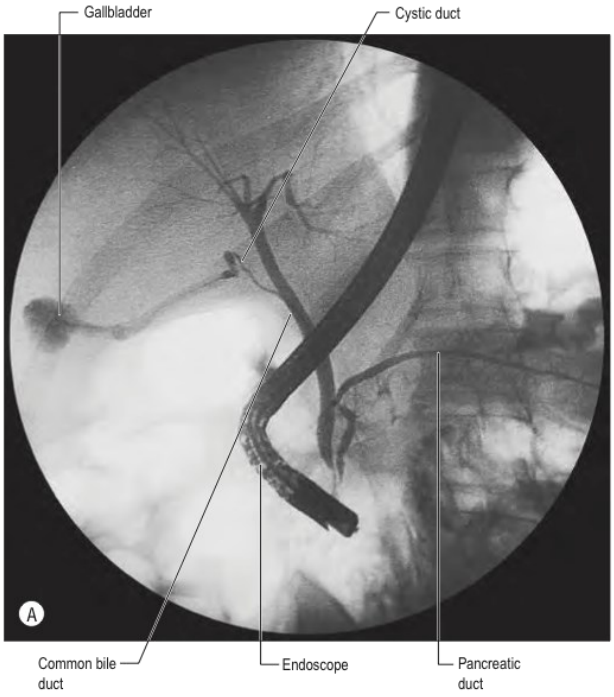

Fig:16 ERCP [7]

8. Operative biliary endoscopy: A flexible choledochoscope is introduced through the cystic duct into the common bile duct to identify and extract gallstones.

9. Percutaneous transhepatic cholangiography[48]: The patient is positioned in a supine position and a short-beveled needle (approximately 12 cm long and 1 mm in diameter) attached to a 20 ml syringe filled with saline is inserted into the abdomen, 2–4 cm below and to the right of the xiphisternum. The needle is directed slightly upwards (cephalad). As it enters the liver, increased resistance is felt, and the patient is instructed to breathe shallowly. Saline is injected to ensure the needle is clear, after which it is advanced 6–8 cm while continuous suction is applied. Once bile is aspirated, contrast medium is injected to assess for biliary stones or intrahepatic abnormalities.

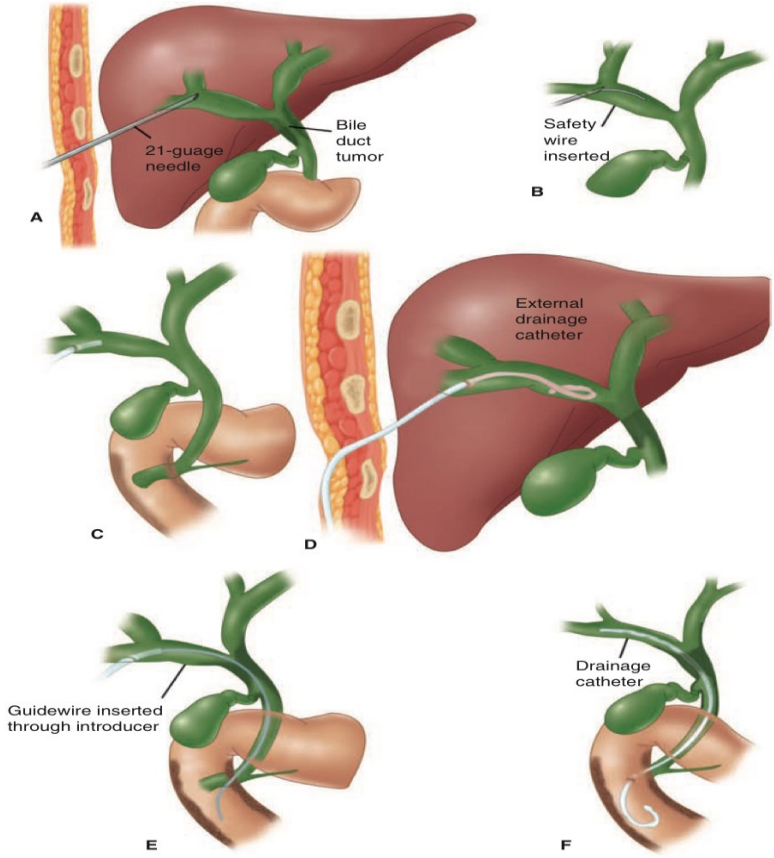

Fig:17 Percutaneous transhepatic cholangiography [48]

10. Blood investigations: This encompasses liver function tests (total bilirubin, direct bilirubin, indirect bilirubin, serum alkaline phosphatase, serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, serum albumin, serum globulin), coagulation profile, serum amylase for pancreatitis, and other regular blood investigations.

TREATMENT

Medical management

1) Oral dissolution:[27]

Cholesterol gallstones have been treated with hydrophilic bile salts, such as ursodeoxycholic acid (UDCA) and chenodeoxycholic acid. Because chenodeoxycholic acid has so many negative consequences, UDCA is preferred.
To sustain hepatic bile acid secretion throughout the night, UDCA is administered at a dose of 10–14 mg/kg OD before bed.

Mechanism of action:

They increase the concentration of bile acids by reducing the release of biliary cholesterol. The cholesterol saturation index is lowered as a result. Bile salts help to reduce inflammation of the gallbladder wall and improve the contractility of the gallbladder's muscles.

2) Indirect dissolution[52]

A percutaneous transhepatic catheter is utilised to infuse 10ml of Methyl tert-butyl ether (MTBE) into the gallbladder. An exchange of this occurs in intervals of 45 minutes. MTBE solubilises cholesterol within 4 to 5 hours. This approach is applicable solely to pure cholesterol stones; however, this approach poses risks to the bile ducts.

3) Mechanical lithotripsy/ Extracorporeal shock wave lithotripsy/ Laser lithotripsy:

- Mechanical lithotriptors are instruments engineered to fragment stones caught within a basket.
- Extracorporeal Shock Wave Lithotripsy (ESWL) has been employed for the treatment of calculi within the gallbladder and the common bile duct by directing shock waves to a specific target point. The solid stones absorb energy and become shattered.
- Lithotripsy can also be performed with laser light.

- Electrohydraulic lithotripsy employs high-voltage electric discharges in brief pulses to generate shock waves, which fragment bile stones for endoscopic removal.

4) Percutaneous cholecystolithotomy: A catheter is introduced into the gallbladder transperitoneally with the help of fluoroscopic guidance or ultrasound guidance under General Anesthesia. Gallstones are disintegrated using lithotripsy and subsequently extracted. Complications encompass Biliary leakage, haemorrhage, pancreatitis.

Surgical management

1) Cholecystostomy[48-52]

This procedure is conducted on patients with acute cholecystitis who are unsuitable for major surgery due to advanced age, renal impairment, or cardiopulmonary disease. The fundus of the gallbladder is incised, and all inflammatory material and calculi are excised. A Foley or Malecot catheter is inserted into the gallbladder and exited by a tiny incision in the belly. The catheter is extracted on the 12th to 15th post-operative day.

2) Cholecystectomy

Surgical removal of gall bladder is known as cholecystectomy.

INDICATIONS:

Symptomatic cholelithiasis

✓ Biliary colic

✓ Acute cholecystitis

Choledocholithiasis

✓ Obstructive jaundice or cholangitis

✓ Gallstone pancreatitis

Asymptomatic cholelithiasis

✓ Sickle cell disease

✓ Chronic immunosuppression

✓ No immediate access to health care

✓ Incidental cholecystectomy for patients undergoing intra-abdominal operations for other reasons

Acalculous cholecystitis

Functional gallbladder disorder

Gallbladder polyps >10 mm

Porcelain gallbladder

a) Laparoscopic cholecystectomy

This procedure is performed under General Anaesthesia with endotracheal intubation.

Patient is positioned supine and a pneumoperitoneum is created using a Veress needle. A periumbilical incision is made through which a 10mm trocar is inserted.

The video camera attached laparoscope is passed through this port. Under direct vision, the next three ports viz. epigastrium, right midclavicular line and right flank are made.

Through the most lateral portal in the flank, an atraumatic grasper is introduced and is used to hold the fundus of gall bladder. The same instrument is used to retract the gallbladder cephalad.

Through the mid-clavicular port, another atraumatic grasper is passed, which is used to hold the infundibulum of gall bladder, to retract it laterally towards the liver's right lower quadrant.

Dissection is done through the epigastric port using a laparoscopic dissector, hook or scissors. After dissecting the hepatoduodenal ligament, the cystic duct and cystic artery are then clipped and divided.

Now the gall bladder is dissected and separated from its fossa. This is now removed from the periumbilical or epigastric incision.

b) Open cholecystectomy[53-54]

Open cholecystectomy is done under general anaesthesia with endotracheal intubation. Positioning of the patient is supine.

Incision can be either a large midline vertical incision or right subcoastal incision (Kocher).

The dissection can be done in three ways:

i. Fundus first method: As the name suggests, first the fundus of the gall bladder is held and mobilized. Following this, the cystic artery is ligated after which the cystic duct is also ligated.

ii. Duct first method: The Calot's triangle is exposed by holding the fundus of gall bladder first, and the Hartman's pouch is held downwards and to the right. The cystic artery and cystic duct are ligated and divided. The gall bladder is subsequently removed.

iii. Mobilization of the hepatic flexure of colon and duodenum to the left.

c) Partial cholecystectomy

The cystic duct and artery are exposed. The contents of gall bladder are evacuated after opening the gall bladder at the fundus. The gall bladder wall is cut from the fundus to the cystic duct leaving a portion of the wall with its mucosa attached to the live

Complications of cholecystectomy [54]

a) Intraoperative
- Vessel injury
- Bile duct injuries
- Bowel injury
- Conversion to laparotomy

b) Postoperative
- Bile/ fluid collection
- Bile leak
- Retained CBD stones

THYROID HORMONES:

PHYSIOLOGY OF THYROID METABOLISM:

The function of the thyroid is intricately linked to iodine metabolism, as the hormones synthesised by the thyroid gland—thyroxine and triiodothyronine—contain a significant proportion of iodine. The effects of these two hormones are fundamentally similar, however they differ significantly in their timing and duration of action. Thyroid hormones are crucial for regulating growth, brain development, and sustaining metabolism and the functional activity of most organs.

Iodine metabolism:[57,58]

Only over 1% of the 5000–8000 μg of iodine contained in a typical thyroid gland is inorganic iodide. About 150 μg of iodine per day is typically consumed through food and drink. In the gut, all iodine is changed into iodide, which is then quickly and fully absorbed into the circulation.

Synthesis of thyroid hormones: [59]

TSH stimulates the synthesis of thyroid hormones by binding to its receptor. The sodium-iodide symporter, NIS, is responsible for the basolateral membrane's uptake of circulating I-. Pendrin is thought to play a role in the process by which intracellular I- accumulates and travels across the apical membrane, supplying this crucial component for hormone production.

Thyroid epithelial cells create Tg, which is then released into the follicular lumen after being processed by the synthetic pathway.

DUOX 2 produces H 2 O 2, which is necessary for the coupling of I- and Tg, at the apical membrane.

TPO catalyzes the reaction between these components; I-coupled to many tyrosine residues within Tg, only a few of which are hormonogenic. There are two types of tyrosine residues: mono- and di-iodinated. These residues can also be coupled by TPO to create the precursors of T3 (mono- + di-iodinated) and T4 (2 × diiodinated). An overview of the prohormone's endocytosis and processing. Before being absorbed, some Tg is proteolyzed at the apical surface by externalized cathepsins. Cathepsins in

lysosomes proteolyze internalized Tg. MCT8, a monocarboxylic acid transporter belonging to the SLC16 family, at least partially mediates the basolateral egress of T3 and T4. Iodotyrosine dehalogenases further break down and recycle unused iodotyrosines.

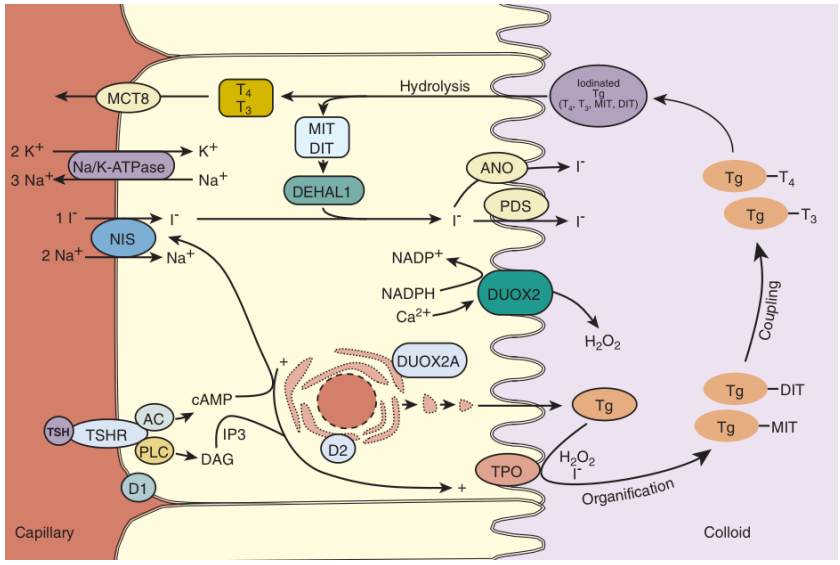

Fig:18 Mechanism of action of thyroid hormone [67]

Storage:

Thyroglobulin stores the thyroid hormones after they are synthesized. There are one to three thyroxine molecules for every thyroglobulin molecule, and on average, there is one tri-iodothyronine molecule for every 14 thyroxine molecules. Thyroid hormones in this form are frequently kept for several months in the follicles. Publication of T4 and T3

Within the endocrine system, the thyroid gland is distinctive in that it has a sizable extracellular area called the follicular lumen, which is used to store hormones and their precursors. The thyroid is distinct from other endocrine glands due to its expansive hormone storage and its sluggish hormone release rate.

Organic iodine in the thyroid gland is composed of the following: T4 makes up about 35%, T3 is about 5%, and iodothyrosines (DIT & MIT) make up around 60%. Thyroid cells' apical surfaces extend around the colloid in the shape of pseudopodia. Thyroglobulin molecules are broken down by the proteinases found in lysosomal enzymes, releasing T3 and T4, which permeate the basement membrane and enter the

bloodstream.

Transportation, turnover and metabolism of thyroid hormone:[59]

Nearly all of T4 and T3 are attached to plasma proteins in the blood, including thyroxine binding albumin (TBA), thyroxine binding globulin (TBG), and thyroxine binding pre-albumin (TBPA). In plasma, 99.98% of T4 is typically protein bound. The level of free T4 is slightly more than 2ng/dL. T4 levels in the urine are quite low. 0.2% (0.3 ng/dL) of the normally present 0.15 g/dL of T3 in plasma is free. Protein binding makes up the remaining 99.8%. Instead than focusing on total hormone concentration, homeostatic management of thyroid function aims to maintain free thyroxine levels. Thyroxine (T4) has a half-life of six days, while T3 has a half-life of one to three days.

About three weeks are stored in the thyroid gland's reserve. TBG has a half-life of roughly five days and a molecular weight of 60,000D. For T4, which is two to six times more than for T3, it has a low capacity but a strong affinity. TBPA has a half-life of roughly two days and a molecular weight of 50,000D. able to bind a lot of T4 and not much T3. For T4 and T3 binding, albumin has a high capacity but a low affinity.

Thyroid hormone protein binding may have the effect of lowering the blood's percentage of free hormones, which in turn lowers loss via the kidneys and liver while preserving the plasma level of free hormones. T4 is more stable in the body than T3 because it is more securely attached to plasma proteins. T3 quickly enters cells and tissue fluids, whereas T4 is an extracellular hormone. Compared to T4, T3 acts faster and has greater potency. T4 functions as a prohormone since it is mostly transformed to T3 by deiodination.

Deiodination to T3 (monodeiodination at the 5' position) or to reverse T3 (monodeiodination at the 5 position) in the liver, kidney, and other locations is the main pathway (85%) of T4 metabolism. Additional pathways include alanine side chain modification to produce acetic or propionic acid and conjugation to produce glucuronides and sulphates.

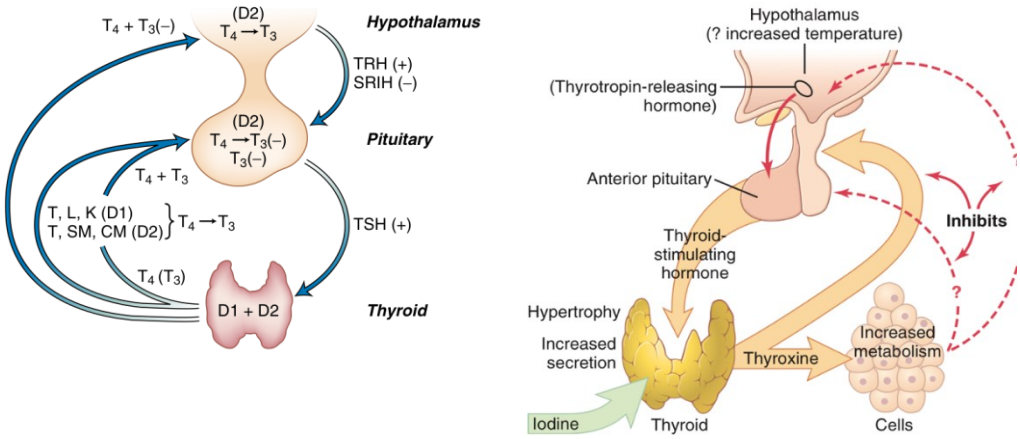

Fig:19 Regulation of thyroid hormone [(64)]

PHYSIOLOGICAL EFFECTS OF THYROID HORMONES ON DIFFERENT BODILY MECHANISMS [60-64]

Thyroid hormones primarily enhance the metabolic activity of most tissues, with exceptions such as the brain, retina, spleen, testes, and lungs. They significantly promote growth in young individuals and trigger various cellular changes, although the exact mechanisms remain largely unclear.

1. Protein Synthesis:

Thyroid hormones stimulate protein synthesis across nearly all tissues, as demonstrated in experimental animal studies.

2. Cellular Enzymes:

They elevate the levels of over 100 intracellular enzymes. For instance, alpha-glycerophosphate dehydrogenase activity can increase up to sixfold.

3. Bone Growth and Calcium Metabolism:

These hormones accelerate bone growth and hasten epiphyseal closure. They also increase osteoclastic activity, leading to elevated excretion of calcium and phosphate via urine and the gastrointestinal tract.

4. Fat and Vitamin Metabolism:

Thyroid hormones enhance all aspects of fat metabolism and increase the body's demand for vitamins.

5. Basal Metabolic Rate (BMR) and Body Weight:

In hyperthyroidism, BMR may rise by up to 100%, often resulting in weight loss despite increased appetite. In contrast, hypothyroidism may reduce BMR to 30–50% of normal levels.

6. Cardiovascular System:

• Increased cardiac output and blood flow

• Elevated heart rate

• Slight rise in blood volume

• Widened pulse pressure

These changes occur in hyperthyroidism, while the opposite is seen in hypothyroidism.

7. Respiratory System:

There is an increase in both the rate and depth of respiration.

8. Gastrointestinal Tract:

Thyroid hormones boost gastrointestinal motility, enhance appetite, and improve absorption of nutrients.

9. Central Nervous System and Sleep:

They heighten mental alertness and synaptic activity but don't affect peripheral nerves. Excess levels can lead to insomnia.

10. Muscles:

High thyroid hormone levels can cause fine muscle tremors at a frequency of 10–15 times per second.

THYROID HORMONES	NORMAL VALUES
T3	0.8- 2 no/ml
T4	5.1 – 14.1 microgram/dl
TSH	0.5 – 5.0 micro /ml

1) Thyroid Function tests:[62-65]

There are numerous tests available to assess thyroid function. For every ailment, no one test is adequate. The clinical state of the patient is taken into consideration while interpreting the data.

Serum Thyroid-Stimulating Hormone (TSH)

Barrett K et al. described the principle of the serum TSH assay as an immunometric technique involving monoclonal antibodies. One antibody, fixed to a solid surface, binds circulating TSH in the sample. A second, labeled monoclonal antibody (tagged with a radioisotope, enzyme, or fluorescent marker) attaches to a different epitope on the TSH molecule.

The sample is incubated for 60 minutes, then washed to remove any unbound labeled antibody. A chemiluminescent substrate is added, and the resulting signal is measured. The intensity of the signal corresponds to the amount of TSH bound by the secondary antibody, indicating serum TSH levels.

Since the anterior pituitary senses circulating free T4 and adjusts TSH secretion accordingly, there is an inverse relationship between TSH and free T4 levels. Even small changes in free T4 can lead to significant shifts in TSH. Therefore, TSH assays are crucial for diagnosing hyperthyroidism, hypothyroidism, and for monitoring and adjusting thyroid hormone replacement therapy.

Total T 4 and T 3 levels

Total T4 and T3 levels are assessed using radioimmunoassay, which measures both the bound and free hormone fractions.

- Total T4 primarily reflects thyroid gland function.

- T3 levels provide insight into the peripheral conversion and metabolism of thyroid hormones.

Causes of Increased Total T4:

1. Hyperthyroidism

2. Elevated thyroglobulin levels, as seen in pregnancy

3. Use of estrogen or progesterone

4. Certain congenital conditions

Causes of Decreased Total T4:

1. Hypothyroidism

2. Use of anabolic steroids

3. Protein-losing conditions, such as nephrotic syndrome

It is important to note that some individuals with low T4 levels may still be clinically euthyroid. In such cases, measuring T3 can help detect early hypothyroidism.

Free T 4 and Free T 3 levels

Radioimmunoassay-based tests offer sensitive detection of biologically active thyroid hormones. However, free T4 measurement is not routinely performed and is primarily reserved for suspected early hyperthyroidism, where total T4 levels may still appear normal, but free T4 levels are elevated. In such cases, free T3 estimation becomes essential for accurate diagnosis.

In Refetoff syndrome (thyroid hormone resistance), there is end-organ resistance to T4. As a result, T4 levels are elevated, but TSH levels remain within the normal range, due to the pituitary's unresponsiveness to the elevated hormone levels.

Free T4 levels are estimated using the T3 resin uptake test. In this method:

- Radiolabeled T3 is introduced into the serum sample.
- If free T4 is elevated, it occupies more of the thyroid hormone binding sites.
- This leaves fewer available sites for T3 binding.

- As a result, more of the radiolabeled T3 binds to the ion-exchange resin, leading to increased T3 resin uptake.

Thyrotropin-Releasing Hormone (TRH)

This test evaluates the pituitary gland's TSH secretion in response to thyrotropin-releasing hormone (TRH). The procedure involves administering 500 µg of TRH intravenously, followed by measuring serum TSH levels at 30 and 60 minutes. A rise in TSH by at least 6 IU/mL indicates a normal pituitary response.

Thyroid Antibodies:

Common thyroid-related antibodies include:

1. Anti-thyroid peroxidase (anti-TPO or antimicrosomal antibodies)

2. Anti-thyroglobulin antibodies

3. Thyroid-stimulating immunoglobulin (TSI)

Anti-TPO and anti-thyroglobulin antibodies do not assess thyroid function directly but serve as markers for autoimmune thyroid disorders, such as Hashimoto's thyroiditis.

- Approximately 80% of Hashimoto's cases present with elevated thyroid antibody levels.
- Increased levels may also be observed in Graves' disease, multinodular goitre, and certain thyroid neoplasms.

Serum Thyroglobulin (Tg)

Thyroglobulin (Tg) is produced by both normal and diseased thyroid tissue and is typically present in the bloodstream in small quantities. However, Tg levels rise significantly during destructive thyroid processes.

Measuring Tg is particularly useful in monitoring patients with differentiated thyroid carcinoma, especially following total thyroidectomy and radioactive iodine (RAI) ablation, as it serves as a marker for recurrence.

It is also important to assess anti-thyroglobulin (anti-Tg) antibodies, as their presence can interfere with Tg measurement and affect the accuracy of results.

Serum Calcitonin

It is a 32-amino-acid polypeptide. It is secreted by C cells. Its functions are to lower serum calcium levels. It is the marker for medullary carcinoma of thyroid.

HYPOTHYROIDISM:[64-69]

Hypothyroidism is a common endocrine disorder, particularly among women. Its subclinical form is notably prevalent in women over 60, affecting up to 20%.

It is characterized by deficient thyroid hormone levels (T3 and T4), which in turn trigger a compensatory rise in TSH due to the body's feedback mechanism. Causes of hypothyroidism include:

- Primary thyroid gland dysfunction
- Pituitary or hypothalamic disorders
- Generalized tissue resistance to thyroid hormone

Common Symptoms:

- Fatigue and weakness
- Dry skin and hair loss
- Weight gain
- Constipation
- Cold intolerance
- Impaired memory and concentration
- Breathlessness
- Hoarseness of voice
- Menstrual irregularities (menorrhagia progressing to oligomenorrhoea or amenorrhoea)
- Tingling or numbness (paraesthesia)

Laboratory Diagnosis

- Primary Hypothyroidism: Elevated TSH with reduced free T4

- Subclinical Hypothyroidism: Elevated TSH with normal free T4 and no obvious symptoms

Prevalence of Hypothyroidism in biliary stone patients:

Epidemiological Evidence:

Numerous studies have established a significant correlation between hypothyroidism (both clinical and subclinical) and gallstone disease:

Inkinen et al. (2001) – Retrospective Study:

- 11% of patients with CBD stones had hypothyroidism
- 6% of gallstone patients without CBD stones had hypothyroidism
- Only 2% in the non-gallstone group had hypothyroidism
- Indicated that reduced bile flow may play a role, not just altered lipid metabolism

Laukkarinen et al. (2007) – Prospective Study:

- Subclinical hypothyroidism was found in 5.3% of gallstone patients vs. 1.4% of controls
- Among women >60 years, 11.4% of gallstone patients had subclinical hypothyroidism vs. 1.8% in controls

Laukkarinen et al. (2010) – Registry-Based Study (Finland):

- 23% of hypothyroid patients had received treatment for gallstones vs. 16% in controls
- 56% of all patients treated for gallstones belonged to the hypothyroid group
- Suggested that gallstone formation might begin during the untreated phase of hypothyroidism

Mechanism of Formation of Gallstones in Hypothyroidism:

Thyroid hormone deficiency affects several physiological processes that predispose to gallstone formation:

1. Altered Bile Composition:

- Reduced cholesterol metabolism leads to cholesterol supersaturation in bile

2. Gallbladder Hypomotility:

- Impaired gallbladder contractility causes bile stasis and promotes cholesterol crystal formation

3. Decreased Bile Secretion:

- Reduced hepatic bile production limits flushing of precipitates from bile ducts

4. Sphincter of Oddi (SO) Dysfunction:

- Hypothyroidism leads to reduced relaxation of SO, causing bile stagnation

Animal and Human Studies on Bile Flow:

- Rat Studies:

Hypothyroid rats showed increased SO tone and reduced bile flow, whereas hyperthyroid rats had enhanced bile secretion.

- Human Study (Post-thyroidectomy):
- In hypothyroid states, hepatic bile clearance and bile flow to the duodenum were reduced.
- Although bile uptake into large ducts remained unchanged, the flow was delayed, attributed to altered bile composition, reduced gallbladder motility, and SO non-relaxation.

Mechanisms by Which Thyroxine Mediates SO Relaxation:

Non-Neural Mechanism:

- Blocking neural pathways (e.g., with tetrodotoxin) did not eliminate thyroxine's relaxing effect on the sphincter, suggesting a direct hormone action.
- Receptor Mediation:
- Sphincter of Oddi cells express thyroid hormone receptors TR β1 and TR β2.
- Although receptor presence alone doesn't confirm action, it supports hormone-mediated relaxation.
- Genomic Mechanism (Delayed Effect):

- Thyroxine binds rapidly to nuclear receptors, but relaxation occurs with a delay, implying gene transcription and protein synthesis are involved.
- Cellular Pathway:
- Activation of potassium channels → causes membrane hyperpolarization
- Inhibition of calcium channels → reduces calcium influx
- Result: Decreased smooth muscle contraction, promoting bile flow

MATERIALS AND METHODS

INCLUSION CRITERIA:

- Patient of any age group or gender who attended outpatient department and patients who are admitted under department of surgery in B.L.D.E. (D. U) Shri B. M. Patil Hospital with cholelithiasis/choledocholithiasis.

EXCLUSION CRITERIA:

- Patients with known thyroid disorders (hypothyroidism or hyperthyroidism), who are on medication or who had undergone any thyroid surgeries.

RESEARCH HYPOTHESIS:

There is increased incidence of cholelithiasis/ choledocholithiasis in patients with hypothyroidism

STUDY DURATION: April 2023 to January 2025

SAMPLING:

With anticipated proportion of Hypothyroidism in diagnosed patients of Gall stones 18.5%[9], the study would require a sample size of minimum 93 patients with 95% level of confidence and 8% absolute precision,

$$n = \frac{z^2 pxq}{d^2}$$

Where Z= Z statistic at α level of significance

d^2= Absolute error

P= Proportion rate

q= 100-p

Statistical Analysis:

- The data obtained will be entered in a Microsoft Excel sheet, and statistical analysis will be performed using statistical package for the social sciences (Version 20).
- Results will be presented as Mean ±SD,Median and interquartile range, frequency, percentages and diagrams.
- Association between Categorical variables will be compared using Chi square test.
- $p<0.05$ will be considered statistically significant. All statistical tests will perform two tailed.

RESULTS AND ANALYSIS:

The study population consisted of 110 patients diagnosed with cholelithiasis or choledocholithiasis. Among them, the highest proportion of patients fell in the 41 to 60 years age group (40%), followed by those above 60 years (26%). A smaller percentage of patients were in the 31 to 40 years category (20%), while the least were below 30 years (14%). This distribution indicates that gallstone disease is more prevalent in middle-aged and elderly individuals, consistent with existing literature on risk factors for cholelithiasis (Table 1)

Table 1: Age Distribution of Patients

Characteristic	**N = 110**[1]
AGE	
31 to 40 years	22 (20%)
41 to 60 Years	44 (40%)
Above 60 years	29 (26%)
Less than 30	15 (14%)
[1] n (%)	

Among the study participants, females accounted for a higher proportion (59%) compared to males (41%). This aligns with the well-established observation that gallstone disease is more common in women, possibly due to hormonal influences such as estrogen's role in cholesterol saturation of bile

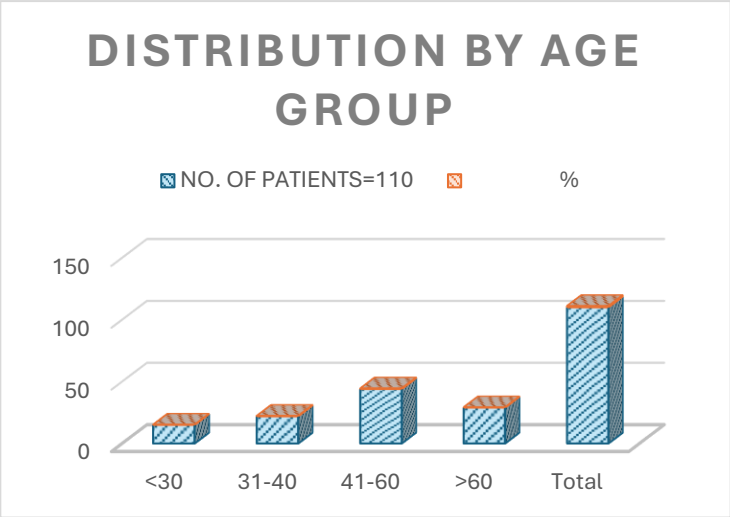

Figure 20: Age Distribution of Patients

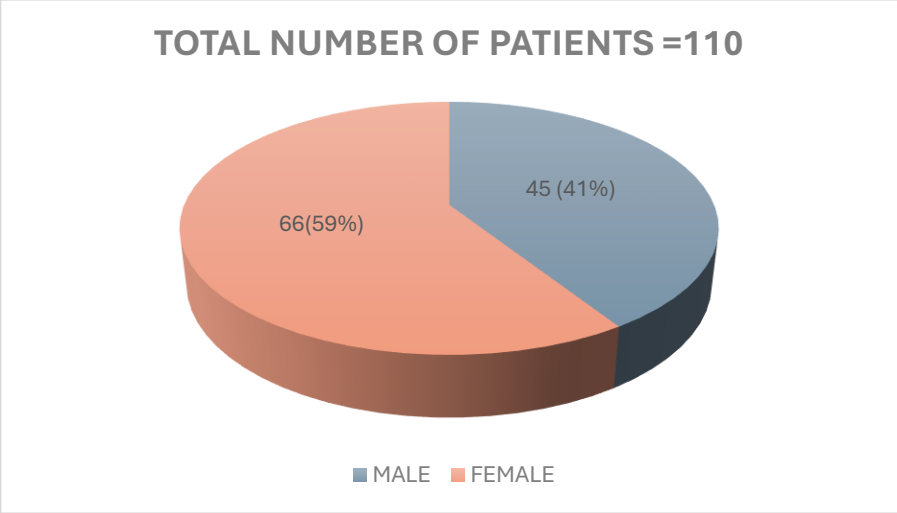

Figure 21: Gender Distribution of Patients

The median (IQR) levels of thyroid hormones in the entire study population were as follows: T3 - 0.96 (0.76, 1.39) ng/mL, T4 - 8.4 (6.3, 10.7) µg/dL, and TSH - 2.99 (1.62, 4.28) µIU/mL. These values provide a baseline reference for evaluating thyroid function in gallstone patients. While median TSH levels are within the normal range, the variability in TSH and free thyroid hormone levels necessitates subgroup analysis.

When comparing thyroid parameters between males and females, T3 levels were found to be slightly lower in females (0.94 vs. 0.98), while T4 levels remained similar (8.4 in both genders). TSH levels were marginally higher in females (3.27 vs. 2.63), though

these differences were not statistically significant ($p > 0.05$). This suggests that while there may be a trend toward higher TSH levels in females, the differences are not pronounced enough to establish a definitive correlation (Table 2).

Table 2: Gender-Based Comparison of Thyroid Function

Characteristic	**Female**, N = 65[1]	**Male**, N = 45[1]	**p-value**[2]
T3	0.94 (0.78, 1.35)	0.98 (0.71, 1.64)	>0.9
T4	8.4 (6.4, 10.7)	8.4 (6.1, 10.5)	0.8
TSH	3.27 (1.63, 4.60)	2.63 (1.60, 4.13)	0.3
[1] n (%); Median (IQR)			
[2] Pearson's Chi-squared test; Wilcoxon rank sum test			

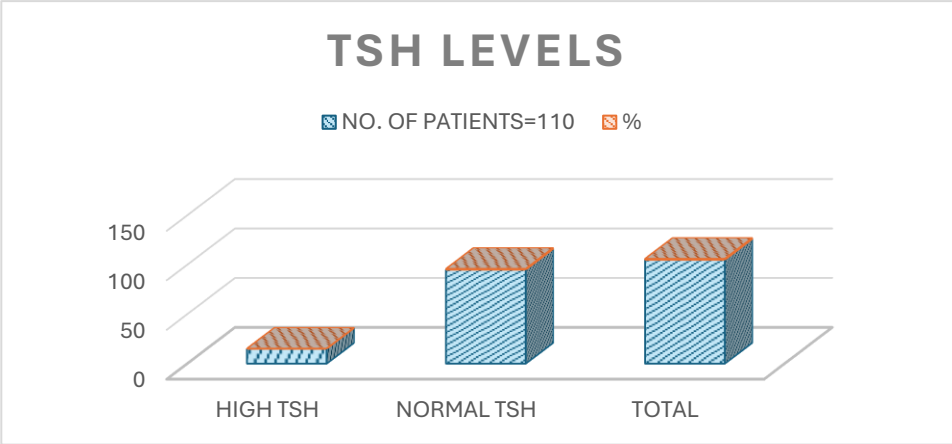

Figure 22: Thyroid Function Parameters in the Study Population

Upon analyzing thyroid function across different age groups, younger patients (<30 years and 31-40 years) exhibited higher T3 levels compared to older patients. The highest median T3 was seen in the 31 to 40 years group (1.20), while it was lowest in those above 60 years (0.88). T4 levels did not show significant variation across age groups. TSH levels were relatively higher in younger patients, with a slight decline in the 41-60 age group before rising again in the elderly. However, none of these variations

were statistically significant ($p > 0.05$), indicating that age alone does not significantly impact thyroid dysfunction in gallstone patients (Table 3).

Table 3: Age-Based Comparison of Thyroid Function

Characteristic	**31 to 40 years**, N = 22[1]	**41 to 60 Years**, N = 44[1]	**Above 60 years**, N = 29[1]	**Less than 30**, N = 15[1]	**p-value**[2]
T3	1.20 (0.82, 1.74)	0.94 (0.76, 1.28)	0.88 (0.67, 1.12)	1.24 (0.84, 1.61)	0.074
T4	8.6 (7.2, 10.6)	8.3 (6.4, 10.9)	8.2 (5.2, 10.5)	8.4 (6.3, 9.6)	0.7
TSH	3.37 (2.05, 4.75)	2.69 (1.45, 3.88)	3.01 (1.40, 4.41)	3.21 (2.08, 3.77)	0.7
[1] n (%); Median (IQR)					
[2] Pearson's Chi-squared test; Kruskal-Wallis rank sum test					

DISCUSSION

The relationship between hypothyroidism and gallstone diseases, such as cholelithiasis and choledocholithiasis, has been a subject of extensive research. Our study observed a higher prevalence of gallstone disease among females (59%) compared to males (41%), aligning with existing literature that indicates a higher incidence in women. This female predominance is consistent with other studies, such as one that reported 66% female and 34% male distribution among gallstone patients.[4]

Regarding thyroid function, our study found that 13% of patients with gallstone disease had hypothyroidism. This prevalence is comparable to other studies. For example, Ahmad MM et al. reported a 12% prevalence of hypothyroidism in biliary tract stone patients [65],and Laukkarinen et al. found a 10.2% prevalence in common bile duct stone patients [66] . Similarly, J Inkinen et al. reported a 10.6% prevalence of hypothyroidism in their study population [67], and Henry Völzke et al. observed a 2.8% prevalence of hypothyroidism in a large cohort of 1500 patients [4]

The pathophysiological mechanisms linking hypothyroidism to gallstone formation include alterations in lipid metabolism, reduced bile flow, and impaired relaxation of the sphincter of Oddi. Hypothyroidism can lead to dyslipidemia, resulting in cholesterol supersaturation in bile, a key factor in cholesterol gallstone formation. Additionally, thyroid hormones influence the motility of the biliary tract; their deficiency may impair the relaxation of the sphincter of Oddi, leading to biliary stasis and subsequent stone formation.

The age distribution of gallstone disease and hypothyroidism varies across studies. Our study found a predominance of gallstone disease in the 41-60 years age group, whereas other studies, such as those by Laukkarinen et al. and Inkinen et al., reported a higher prevalence in patients above 60 years [66,67]. Ahmad MM et al. noted that 66% of their study population with gallstones and hypothyroidism were between 51 and 60 years of age [65] .Kulkarni V et al. observed a male predominance in hypothyroid patients with gallstones, whereas most other studies, including ours, found a higher prevalence among females [68] .

However, not all studies have found a significant association between hypothyroidism and gallstone disease. For example, some studies concluded that there was no significant

relationship between thyroid hormone disorders and cholelithiasis [69,70]. These discrepancies may be due to differences in study design, population characteristics, and sample sizes.

While this study provides valuable insights into the association between hypothyroidism and gallstone disease, certain limitations must be acknowledged. The study is based on a single-center dataset, limiting the generalizability of findings to broader populations. The sample size, though adequate, may not be large enough to detect small but clinically significant differences. Confounding factors such as diet, obesity, and lifestyle habits, which are known to contribute to both thyroid dysfunction and gallstone disease, were not comprehensively accounted for. The study design is cross-sectional, preventing the establishment of a causal relationship between hypothyroidism and gallstone disease. Additionally, the study did not differentiate between different types of gallstones, which may have distinct pathophysiological mechanisms.

LIMITATIONS OF THE STUDY

- Small sample size
- It is a cross sectional study
- Only patients diagnosed with gallstone diseases are taken in to consideration.
- Patients with known hypothyroidism were not evaluated for gall stone disease.

CONCLUSION

Our findings support the association between hypothyroidism and gallstone diseases, particularly among females and middle-aged individuals. Thyroid dysfunction may contribute to gallstone formation through mechanisms such as dyslipidemia, reduced bile flow, and impaired sphincter of Oddi relaxation. Given the potential impact of thyroid dysfunction on gallstone formation, it is crucial to consider thyroid screening in patients with gallstone disease. However, further research is needed to clarify the nature of this association and the potential benefits of early thyroid intervention.

RECOMMENDATIONS

Based on the findings of this study, the following recommendations are proposed:

- Routine thyroid function screening should be considered for patients diagnosed with gallstone disease, particularly those with risk factors such as dyslipidemia and obesity.
- A multicenter, large-scale prospective study should be conducted to further validate the association between hypothyroidism and gallstone disease.
- Future studies should explore the impact of thyroid hormone replacement therapy in patients with gallstone disease and underlying thyroid dysfunction.
- Public health initiatives should focus on educating patients about the potential link between thyroid health and gallstone formation to encourage early diagnosis and management.

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A CLINICAL STUDY ON THE PRESENCE OF HYPOTHYROIDISM IN PATIENTS WITH GALLSTONES

PROFORMA

CASE NUMBER: **IP NUMBER:**

NAME: **OPD NUMBER:**

AGE/SEX: **WARD/UNIT:**

OCCUPATION: **DATE OF ADMISSION:**

ADDRESS: **DATE OF DISCHARGE:**

CHIEF COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

TREATMENT HISTORY:

SURGICAL HISTORY:

PERSONAL HISTORY:

Dietary
Habits-
Appetite-
Sleep-

Bowel and bladder
habits- Habits-

GENERAL PHYSICAL EXAMINATION:

BUILT: Well/ Moderate/ Poor

NOURISHMENT: Well/ Moderate / Poor

WEIGHT: kg, HEIGHT: cm, BMI: kg/m^2

PALLOR- ICTERUS- CYANOSIS- CLUBBING-

PEDAL EDEMA- GENERALISED LYMPHADENOPATHY-

VITALS:

Temperature -

Pulse -bpm

Blood Pressure - mmHg, Respiratory Rate CPM

LOCAL EXAMINATION:

SYSTEMIC EXAMINATION:

RESPIRATORY SYSTEM:

CARDIOVASCULAR SYSTEM: CENTRAL

NERVOUS SYSTEM:

CLINICAL DIAGNOSIS:

INVESTIGATIONS:

USG ABDOMEN AND PELVIS:

Impression:

THYROID PROFILE:

T3		
T4		
TSH		

COMPLETE HEMOGRAM:

HB	
PCV	
RBC	
TC	
PLATELET	

COMPLETE URINE ROUTINE :

COLOUR	
APPEARANCE	
SUGAR	
ALBUMIN	
PUS CELLS	
EPITHELIAL CELLS	
RBC	

LIPID PROFILE:

TOTAL CHOLESTEROL	
LDL	
VLDL	
HDL	
TRIGLYCERIDES	

LIVER FUNCTION TEST:

TOTAL BILIRUBIN	
CONJUGATED	
UNCONJUGATED	
SGPT	
SGOT	
SE PROTEIN	
SE ALBUMIN	
GLOBULIN	
AG RATIO	
ALP	

CT ABDOMEN AND PELVIS:

Impression:

TREATMENT FOR THYROID DISORDERS:

CONSERVATIVE	
THYROIDECTOMY	

SURGICAL PROCEDURES:

OPEN CHOLECYSTECTOMY	
LAPAROSCOPIC CHOLECYSTECTOMY	
CHOLEDOCHOLITHOTOMY	
PERCUTANEOUS CHOLECYSTOTOMY	
CBD EXPLORATION	
ERCP	
MRCP	
T TUBE	

Ethical Clearance Certificate

BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 917/2023-24 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinized the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "A CLINICAL STUDY ON THE PRESENCE OF HYPOTHYROIDISM IN PATIENTS WITH GALLSTONES".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.SRI VENKATA CHALLA

NAME OF THE GUIDE: DR.TEJASWINI VALLABHA, PROFESSOR, DEPT. OF GENERAL SURGERY.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
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BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
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MASTER CHART

Sl. Number	IP. Number	Age	Sex	Symptoms of Hypothyroidism					Co-Morbidities	Thyroid Examination	Thyroid Function Test			Ultrasonography of Abdomen			Procedure	Remarks	FNAC	Thyroid Management
				Cold Intolerance	Loss of Appetite/Weight gain	Hair Loss	Constipation	Menstural Disturbances			T3	T4	TSH	GB Calculi	CBD Calculi	No. of Calculi				
1	133669	45	M	-	-	-	-	-	DM	NORMAL	0.98	11.36	1.828	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
2	118502	51	F	-	-	-	-	-	NIL	NORMAL	1.04	8.12	2.796	+	+	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
3	97506	45	M	-	-	-	-	-	HTN	NORMAL	0.82	7.54	2.52	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
4	133977	24	F	-	-	-	-	-	NIL	NORMAL	0.73	9.2	0.67	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
5	126884	44	M	-	-	-	-	-	HTN	NORMAL	0.98	6.3	0.861	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
6	206941	61	F	-	-	-	-	-	DM, HTN	NORMAL	0.95	7.8	3.866	+	+	Multiple	CBD Exploration	Euthyroid	-	-
7	35963	46	M	-	-	-	-	-	NIL	NORMAL	0.87	11.72	0.616	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
8	181550	64	F	-	-	-	-	-	DM	NORMAL	0.77	10.52	1.967	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
9	178910	23	F	-	-	-	-	-	NIL	NORMAL	0.68	15.58	4.048	+	-	Multiple	CBD Exploration	Euthyroid	-	-
10	178105	43	M	-	-	-	-	-	HTN	NORMAL	0.18	10.35	4.393	+	+	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
11	146044	44	F	-	-	-	-	-	NIL	NORMAL	0.9	8.28	0.529	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
12	188791	40	F	-	-	-	-	-	NIL	NORMAL	0.79	12.41	2.42	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
13	193168	35	F	+	-	-	+	+	NIL	NORMAL	1.1	12.81	5.357	+	-	Multiple	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
14	200176	52	F	-	-	-	-	-	DM	NORMAL	0.86	7.54	2.5	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
15	206995	60	F	-	-	-	-	-	DM	NORMAL	0.81	11.41	1.066	+	+	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
16	197300	56	F	-	-	-	-	-	HTN	NORMAL	1.38	12.48	5.8	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
17	206668	56	M	-	-	-	-	-	HTN	NORMAL	0.9	10.7	1.6	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
18	185998	72	F	+	-	+	+	-	DM	NORMAL	1.03	9.39	6.8	+	-	Multiple	-	Subclinical Hypothyroidism	-	-
19	200469	60	F	-	-	-	-	-	NIL	NORMAL	0.56	10.65	1.528	+	+	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
20	260379	50	F	+	+	-	+	-	NIL	NORMAL	0.65	5.31	5.641	+	-	Single	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
21	247767	48	F	-	-	-	-	-	NIL	NORMAL	0.821	6.4	2.13	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
22	267921	46	F	-	-	-	-	-	DM	NORMAL	1.03	11.11	3.535	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
23	340867	68	M	-	-	-	-	-	DM, HTN	NORMAL	2.1	5.82	1.65	+	-	Single	-	Euthyroid	-	-
24	270733	60	F	-	-	-	-	-	HTN	NORMAL	1.5	12.11	3.578	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
25	254049	36	M	-	-	-	-	-	NIL	NORMAL	1.74	7.6	4.6	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
26	231560	33	M	-	-	-	-	-	NIL	NORMAL	0.85	8.15	3.246	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
27	288781	38	M	-	-	-	-	-	HTN	NORMAL	0.38	10.49	0.575	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
28	305848	42	F	-	-	-	-	-	NIL	NORMAL	0.91	4.2	1.61	+	-	Multiple	-	Euthyroid	-	-
29	44280	29	F	-	-	-	-	-	NIL	NORMAL	1.86	6.42	1.631	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
30	335029	90	M	-	-	-	-	-	NIL	NORMAL	0.72	12.18	1.649	+	+	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
31	270835	65	M	-	-	-	-	-	DM	NORMAL	0.86	10.88	1495	+	-	Multiple	-	Euthyroid	-	-
32	339955	70	F	-	-	-	-	-	DM	NORMAL	0.48	11.79	1.361	+	+	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
33	340994	32	F	+	-	-	+	+	NIL	NORMAL	1.2	8.4	18.834	+	-	Single	Laparoscopic Cholecystectomy	Overt Hypothyroidism	-	-
34	30261	75	M	-	+	+	-	-	HTN	NORMAL	2.1	6.4	8.2	+	-	Multiple	-	Subclinical Hypothyroidism	-	-
35	311577	66	M	-	-	-	-	-	DM, HTN	NORMAL	0.96	8.56	4.412	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
36	372393	34	F	-	-	-	-	-	Bronchial Asth	NORMAL	2.1	6.43	4.2	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
37	85819	23	F	-	-	-	-	-	NIL	NORMAL	3.2	6.1	3.5	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
38	29298	86	F	-	-	-	-	-	NIL	NORMAL	1.07	4.8	3.1	+	+	Single	CBD Exploration	Euthyroid	-	-
39	377732	24	F	-	-	-	-	-	NIL	NORMAL	0.86	10.05	2.581	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
40	331223	56	F	-	-	-	-	-	HTN	NORMAL	0.76	15.01	0.539	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
41	102589	57	M	-	-	-	-	-	NIL	NORMAL	2.63	8.2	0.643	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
42	312314	33	F	+	-	-	+	+	NIL	NORMAL	5.2	8.6	20.1	+	-	Single	-	Overt Hypothyroidism	-	Thyroxine
43	201011	53	M	-	-	-	-	-	DM	NORMAL	0.57	9.05	2.456	+	+	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
44	16416	55	M	-	-	-	-	-	DM, HTN	NORMAL	2.3	9.9	0.424	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
45	14999	55	M	-	-	-	-	-	DM, HTN	NORMAL	2.3	0.7	0.962	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
46	28434	74	F	-	-	-	-	-	NIL	NORMAL	0.91	8.5	3.454	+	+	Multiple	CBD Exploration	Euthyroid	-	-
47	14791	19	M	-	-	-	-	-	NIL	NORMAL	1.8	0.42	3.21	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
48	324242	70	F	-	-	-	-	-	DM	NORMAL	1.32	3.51	1.4	+	+	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
49	34274	24	F	-	-	-	-	-	NIL	NORMAL	0.81	8.4	4.2	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
50	245517	45	M	+	+	-	-	-	HTN	NORMAL	2.3	5.6	11.21	+	-	Multiple	-	Overt Hypothyroidism	-	Thyroxine
51	406479	46	F	+	-	-	+	+	NIL	NORMAL	1.6	6.5	8.2	+	-	Single	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
52	80308	42	M	-	+	+	+	-	NIL	NORMAL	0.56	9.32	6.01	+	-	Multiple	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
53	300166	37	F	-	-	-	-	-	NIL	NORMAL	3.2	6.3	4.8	+	-	Multiple	-	Euthyroid	-	-
54	84894	22	F	-	-	-	-	-	NIL	NORMAL	1.4	8.5	5.21	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
55	85351	59	M	-	-	-	-	-	NIL	NORMAL	0.53	7.9	3.383	+	-	Single	-	Euthyroid	-	-
56	58479	47	M	-	-	-	-	-	HTN	NORMAL	0.76	10.81	2.016	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
57	80318	55	M	-	-	-	-	-	HTN, DM, CAD	NORMAL	1.6	8.4	4.78	+	+	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
58	94306	72	M	-	-	-	-	-	NIL	NORMAL	2.1	0.7	2.199	+	-	Single	-	Euthyroid	-	-
59	68097	72	M	-	-	-	-	-	HTN	NORMAL	1.8	0.9	1.2	+	-	Multiple	-	Euthyroid	-	-
60	78685	38	F	-	-	-	-	-	Bronchial Asth	NORMAL	1.41	10.97	2.091	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
61	95724	36	F	-	-	-	-	-	NIL	NORMAL	1.65	10.7	2.031	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
62	118347	73	F	+	+	-	-	+	NIL	NORMAL	1.53	4.7	6.12	+	+	Multiple	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
63	118175	64	M	-	-	-	-	-	HTN	NORMAL	0.79	8.2	3.21	+	-	Multiple	-	Euthyroid	-	-
64	256584	58	F	-	-	-	-	-	DM	NORMAL	0.61	2.53	4.72	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
65	116160	34	F	-	-	-	-	-	NIL	NORMAL	0.82	3.6	3.78	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
66	125201	29	F	-	-	-	-	-	NIL	NORMAL	0.71	5.3	4.72	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
67	131008	42	F	-	-	-	-	-	NIL	NORMAL	1.32	11.98	1.983	+	+	Multiple	CBD Exploration	Euthyroid	-	-
68	18408	52	M	-	-	-	-	-	CAD	NORMAL	1	11.01	3.3	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
69	19707	36	M	-	-	-	-	-	NIL	NORMAL	1.84	10.54	4.6	+	-	Multiple	-	Euthyroid	-	-
70	361243	46	F	+	-	-	+	-	DM	NORMAL	0.94	9.92	7.32	+	-	Multiple	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
71	26440	71	M	-	+	-	-	+	HTN	NORMAL	0.61	1.65	7.521	+	-	Multiple	-	Subclinical Hypothyroidism	-	-
72	162311	31	M	-	-	-	-	-	NIL	NORMAL	2.3	10.23	1.2	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
73	77200	73	M	-	-	-	-	-	NIL	NORMAL	1.26	5.2	4.3	+	+	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
74	258956	70	F	-	-	-	-	-	DM	NORMAL	1.51	11.55	1.343	+	-	Multiple	-	Euthyroid	-	-
75	265589	46	F	-	-	-	-	-	HTN	NORMAL	1.3	7.3	3.66	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
76	172248	36	F	+	-	+	-	+	NIL	NORMAL	0.51	8.2	5.86	+	-	Multiple	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
77	158850	62	M	-	-	-	-	-	HTN	NORMAL	0.3	13.84	1.3	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
78	163333	30	M	-	-	-	-	-	NIL	NORMAL	1.23	8.72	2.046	+	-	Single	-	Euthyroid	-	-
79	127616	37	F	-	-	-	-	-	NIL	NORMAL	0.73	10.65	0.286	+	-	Single	-	Euthyroid	-	-
80	18756	55	M	-	-	-	-	-	HTN	NORMAL	1.26	12.19	4.131	+	-	Multiple	-	Euthyroid	-	-
81	27555	52	F	-	-	-	-	-	DM, HTN	NORMAL	0.9	10	1.2	+	+	Multiple	-	Euthyroid	-	-
82	125262	32	F	-	-	-	-	-	HTN	NORMAL	1.06	9.41	2.896	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
83	184453	18	M	-	-	-	-	-	NIL	NORMAL	1.42	6.4	2.63	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
84	197991	74	F	-	-	-	+	-	DM	NORMAL	0.89	2.41	5.921	+	-	Multiple	-	Subclinical Hypothyroidism	-	-
85	201960	26	F	-	-	-	-	-	NIL	NORMAL	1.8	0.42	3.21	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
86	223056	38	F	-	-	-	-	-	NIL	NORMAL	1.32	3.51	1.4	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
87	85760	64	F	-	-	-	-	-	DM	NORMAL	0.414	10.68	0.64	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
88	220472	32	F	-	-	-	-	-	NIL	NORMAL	1	11.43	1.194	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
89	234629	79	F	-	-	-	-	-	NIL	NORMAL	0.56	11.52	0.219	+	+	Multiple	CBD Exploration	Euthyroid	-	-
90	235869	38	F	-	-	-	-	-	DM, HTN	NORMAL	Jan-00	7.09	2.716	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
91	128359	27	F	-	-	-	-	-	NIL	NORMAL	1.37	8.31	1.72	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
92	126350	43	F	-	-	-	-	-	NIL	NORMAL	1.08	6.31	4.2	+	+	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
93	235863	36	F	-	-	-	-	-	NIL	NORMAL	0.62	8.52	3.5	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
94	254897	53	M	-	-	-	-	-	NIL	NORMAL	0.76	6.32	3.1	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
95	221586	55	M	-	-	-	-	-	HTN	NORMAL	1.32	5.38	2.581	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
96	225898	32	F	+	-	-	+	+	NIL	NORMAL	1.08	4.26	5.92	+	-	Multiple	Laparoscopic Cholecystectomy	Subclinical Hypothyroidism	-	-
97	236541	80	M	-	-	-	-	-	NIL	NORMAL	0.69	6.1	3.8	+	-	Multiple	-	Euthyroid	-	-
98	236598	78	M	-	-	-	-	-	HTN	NORMAL	0.52	5.82	3.005	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
99	212123	41	M	-	-	-	-	-	DM	NORMAL	1.06	13.14	0.904	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
100	256893	56	M	-	-	-	-	-	DM, HTN	NORMAL	1.06	10.15	0.729	+	-	Single	-	Euthyroid	-	-
101	215632	73	M	-	-	-	-	-	HTN	NORMAL	0.48	9.31	2.84	+	+	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
102	254856	45	M	-	-	-	-	-	DM	NORMAL	0.55	4.01	2.98	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
103	258987	44	F	-	-	-	-	-	NIL	NORMAL	0.33	5.34	3.269	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
104	230215	28	F	-	-	-	-	-	NIL	NORMAL	0.91	10.98	3.32	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
105	220369	30	M	-	-	-	-	-	NIL	NORMAL	1.24	13.14	2.12	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
106	221401	45	F	-	-	-	-	-	DM	NORMAL	1.41	7.71	[illegible]	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
107	235654	45	F	-	-	-	-	-	NIL	NORMAL	0.61	5.6	3.31	+	-	Multiple	Laparoscopic Cholecystectomy	Euthyroid	-	-
108	213601	38	F	-	-	-	-	-	NIL	NORMAL	0.51	7.51	4.75	+	-	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
109	225800	65	F	-	-	-	-	-	NIL	NORMAL	0.82	8.96	1.262	+	+	Single	Laparoscopic Cholecystectomy	Euthyroid	-	-
110	214587	80	M	-	-	-	-	-	HTN	NORMAL	0.55	4.01	2.98	+	-	Multiple	-	Euthyroid	-	-

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